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Title of Dissertation: "Understanding Obesity and the Influence of Acculturation on Metabolic Responses in East Asian Populations in the United States"

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Doctor of Philosophy Degree
29 August 2007

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Abstract

Title of Dissertation: Understanding Obesity and the Influence of Acculturation on Metabolic Responses in East Asian Populations in the United States

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The relationship between obesity and weight-related health consequences may differ by ethnicity. East Asians are predisposed to develop centralized obesity and insulin resistance, which are the two major risk factors for diabetes. Furthermore, a diet high in fat and a lack of physical activity, which characterize Western lifestyle, may have a severe negative impact on metabolic consequences in East Asians in the United States. The first aim of this study was to compare anthropometric measures and metabolic responses both at fasting and in response to a naturalistic meal. The second aim focused on East Asians, was to examine the contribution of acculturation to metabolic responses in a path analysis to connect acculturation, diet and physical activity, body weight, and insulin responses.

Healthy East Asian men and women (n=37) and European descent Caucasians (n=40) were recruited to participate in a study of body weight and insulin response. Anthropometric, glucose, and insulin measures were obtained during a

laboratory visit for all participants. East Asians also completed an acculturation questionnaire and monitored dietary and physical activities for 3 days.

Results indicated that East Asians were hyperglycemic and hyperinsulinemic in response to a standardized meal although no apparent interethnic differences were found in anthropometric measures and fasting glucose and insulin concentrations. The hyperinsulinemic response was positively associated with BMI and negatively associated with exercise, as expected. However, more acculturated individuals reported higher physical activity although their BMI was higher. The results highlight the direct positive effect of exercise on improving insulin response and the indirect negative effect of a diet high in fat on insulin response via body weight gain. Differences in exercise habits between East Asians and Caucasians partially explained the differing postprandial metabolic responses. East Asian ethnicity is a risk factor for insulin resistance. Efforts to reduce body weight and insulin resistance in this group should be a primary public health target. Particularly, community outreach programs encouraging regular exercise, specifically targeting normal weight recent immigrants, is necessary to increase the fitness of East Asian groups and to reduce the ethnic health disparity in the U.S.

Understanding Obesity and the Influence of Acculturation on Metabolic Responses in East Asian Populations in the United States

BY

Su-Jong Kim, M.S.

Dissertation submitted to the Faculty of the

Department of Medical and Clinical Psychology

of the Uniformed Services University of the Health Sciences

in partial fulfillment of the requirements for the degree of

Doctor of Philosophy,

2007

Acknowledgements

I would like to take this opportunity to thank all of the members of my dissertation committee for their involvement on this project. I thank David S. Krantz, Ph.D. for serving as a committee chairman and providing insightful feedback on methodology. Willem J. Kop, Ph.D. always offered professional supported when needed. Patricia A. Deuster, Ph.D. MPH. provided me with all the resources I needed in conducting this project at the Human Performance Laboratory (HPL). I am indebted to Dr. Deuster for her valuable professional support and knowledge in exercise physiology. Tracy Sbrocco, Ph.D. served as my advisor for the duration of my dissertation work. I thank Dr. Sbrocco for encouraging me to pursue the research topic of my interest and to always remember the reason why I am in the field of Psychology.

I would also like to thank the people I met at USUHS for their professional and personal support. Nicole Fendrick and Stacey Zeno at the HPL provided me with unlimited technical support and encouragement. Ali Weinstein, Ph.D. has been a wonderful colleague and a very close friend from the first day at USUHS. I appreciate her friendship that went beyond the class-room. I would also like to thank Joyce Hsiao for statistical consultation. Without her, my understanding of statistics and application of it would have been much more limited. I would like to extend my appreciation to Alan T. Remaley, M.D., Ph.D., in the Department of Laboratory Medicine at the NIH for conducting assay for my samples. Finally, I thank my husband, Robert W. Dorner, Ph.D., for reading my dissertation many, many, times and asking insightful questions. I could not have done it without you.

This project is dedicated to my family in Korea and in the United States.

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1. Introduction

East Asians[1] have been commonly considered to be *thin* and free of weight-related health problems. Recent data show that the prevalence of overweight and obesity in East Asians has increased (Gu et al., 2005; James, Leach, Kalamara, & Shayeghi, 2001; D. M. Kim, Ahn, & Nam, 2005). Moreover, East Asians develop obesity related diseases, such as type 2 diabetes mellitus (T2DM), at much lower body weights than Caucasians (Fujimoto, 1995; McNeely & Boyko, 2004). Central obesity and insulin resistance, two major risk factors of T2DM, may be responsible for the development of T2DM in East Asians without obvious peripheral obesity. However, the relationship between increasing body weight and insulin resistance is poorly understood in East Asian populations in the U.S. The characterization of the relationship between body weight and insulin resistance may be important for understanding the development and progression of T2DM in East Asians, which cannot be comprehended by a Caucasian-centric understanding of obesity and related disease development.

A Western lifestyle, characterized by high fat consumption and physical inactivity, may be a key factor that intensifies the course of T2DM development through weight gain and insulin resistance in East Asians. Little is known, however, about how acculturation to a Western lifestyle in East Asians in the U.S. affects the diet and physical activity and in turn the metabolic consequences. As the number of East Asians increases in the U.S., such information becomes crucial to

[1] "East Asian" refers only to people of Chinese, Korean, or Japanese origin whereas "Asians" refers to all individuals from Asian countries including South Asia, Southeast Asia, and East Asia. These two terms are not interchangeable and the distinction will remain consistent throughout this dissertation.

understanding the increasing prevalence of overweight/obesity, insulin resistance, and T2DM in East Asians as a result of adopting a Western lifestyle.

The goals of the current investigation were to: (1) Examine the relationship of body weight (e.g., anthropometric measures) and metabolism (e.g., glucose, insulin, and insulin resistance) during the fasting state and postprandial in East Asians compared to Caucasians; and (2) Examine the influence of acculturation via mediating behavioral factors (i.e., dietary and physical activity pattern) on the insulin responses in the East Asian group. The central hypotheses of this study were that East Asians would have more abdominal fat and would be more insulin resistant compared to Caucasians of comparable body mass index (BMI); and that an increasing level of acculturation would be associated with increasing insulin resistance in East Asians. The following sections provide an overview of obesity and diabetes, insulin resistance, and dietary and physical activity patterns specific to East Asians.

2. Background

2.1. Obesity and Diabetes

2.1.1. Definition and Prevalence of Obesity

The World Health Organization (WHO) defines obesity as a condition of excessive fat accumulation in the body to the extent that health and well-being are adversely affected. One of the most frequently used methods to estimate the degree of excessive body fat is the BMI; a weight adjusted for height scale (kg/m^2). The National Heart, Lung, and Blood Institute (NHLBI) and WHO BMI define overweight as a BMI of 25-29.9 kg/m^2 and obesity as a BMI ≥ 30 kg/m^2 (NIH, 1998; WHO, 1995). Based on these BMI classifications, results from the 1999-2002 National Health and Nutrition Examination Survey (NHANES) indicate that 65% of the adult population in the U.S. was overweight and about 30% was obese. This figure reflects over a 100% increase in obesity prevalence during the past two decades.

2.1.2. Definition and Prevalence of Type 2 Diabetes Mellitus

During the 20th century, chronic diseases became the leading cause of mortality in the U.S. (WHO, 2003a). Recent data show that up to 70% of all deaths occurring in the U.S. are related to cardiovascular disease (CVD), diabetes, and cancer (Arias, Anderson, Kung, Murphy, & Kochanek, 2003). Particularly in the case of T2DM, the prevalence has increased 600% from 1958 to 1993 (ADA, 1996), and the number is still rising (Mokdad et al., 2001; Mokdad et al., 2003).

Diabetes is a chronic condition associated with abnormally high levels of the glucose in the blood. There are two types of diabetes: type 1 and type 2 diabetes mellitus. T2DM results from a progressive insulin secretory defect on the background of insulin resistance whereas type 1 diabetes results from β-cell destruction, which usually leads to absolute deficiency of insulin (ADA, 2007). For this reason, T2DM develops later in life and the disease onset can be prevented or delayed by health behavior modification alone. Clinical diagnostic criteria for diabetes have changed over time, and according to the most recent guideline, diagnosis of diabetes are made if one of the following conditions are found: (1) Symptoms of diabetes and a causal (random) plasma glucose ≥ 200 mg/dl (11.1 mmol/l); (2) Fating plasma glucose ≥ 126 mg/dl (7.0 mmol/l); or (3) 2 hour plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (bolus of 75g of glucose) (ADA, 2007). Furthermore, fasting plasma glucose between 100 and 125 mg/dl is considered to be impaired fasting glucose, and 2 hour plasma glucose of 140 to 199 mg/dl is impaired glucose tolerance. These two conditions are now officially termed pre-diabetes.

T2DM is a particularly serious ailment because the vast majority of persons with T2DM die from cardiovascular complication, and experience significant reductions in quality of life due to disease complications, such as blindness, kidney failure, and non-traumatic amputations (Schulze & Hu, 2005). The U.S. Center for Disease Control and Prevention (CDC) reports the prevalence of T2DM to be approximately 8% in the U.S. Worldwide, T2DM has increased from affecting approximately 35 million people in 1985 to 171 million in 2000 (WHO, 2003b).

Particularly in the Asian countries, the prevalence of T2DM is soaring. For instance, until recently the prevalence of T2DM was less than 1% in China. However, within the last two decades, a three-fold increase has been witnessed in certain areas of China because of Westernization and the consequent increase in body weight (X. R. Pan et al., 1997). Chinese men and women who live in Hong Kong or Taiwan have a substantially higher prevalence of T2DM than Chinese in mainland China (J. C. Chan & Cockram, 1997), and the Japanese individuals who live in America compared to those in Japan also have a higher rate of T2DM (Fujimoto, 1992). It is clear that T2DM is increasing in East Asians, and the East Asians who reside in industrialized/westernized environment are particularly affected by T2DM.

2.1.3. Relationship between Body Weight and Type 2 Diabetes Mellitus

Excessive body fat is considered to be the single most important risk factor for T2DM (Hu, Manson et al., 2001). Thus, the increasing prevalence of T2DM may reflect increasing body weight. Previous studies have shown that changes in BMI at the population level precede changes in the onset of T2DM (Ford, Williamson, & Liu, 1997; Holbrook, Barrett-Connor, & Wingard, 1989; Resnick, Valsania, Halter, & Lin, 2000). Moreover, modest weight gain during adulthood is also associated with an increased risk of developing T2DM compared to weight stable adults (Colditz, Willett, Rotnitzky, & Manson, 1995). For instance, women who gained 5 ~11 kg during adulthood had a 2~3 fold increased risk of developing T2DM when compared with the weight stable women (gained less than 5 kg). Women who gained 20 kg or more were 12.3 times more likely to develop T2DM compared to people who had not gained weight. In contrast, losing more than 5 kg of body weight reduced the risk of

developing T2DM by 50% or more. Similar results have been found in men. Every kilogram of weight gained was associated with a 7.3% increased risk (Koh-Banerjee et al., 2004).

The relationship between weight gain and the development of T2DM has also been found to be compelling in East Asians. Even small increases in body weight contribute to the development of T2DM (Abate & Chandalia, 2001; McNeely et al., 2001) and T2DM worsens progressively with additional weight gain in East Asians (W. H. Pan et al., 2004). Furthermore, the risk of having T2DM is high even in normal weight East Asian adults (Jia, Xiang, Chen, Lu, & Wu, 2002). Increases in body weight are associated with an increasing prevalence of T2DM in both genders and across different racial groups. However, East Asians seem to have a lower body weight threshold for developing T2DM. If so, then investigating the relationship between body weight and its related health consequences in East Asians in the U.S. is necessary because (1) East Asians suffer from weight-related health consequences despite initial beliefs that East Asians were free from obesity related negative health outcomes, (2) East Asians in the U.S. have greater odds of developing T2DM compared to those in their native countries because of a obesity and T2DM promoting lifestyle; and (3) East Asians seem to suffer from obesity-related health problems at lower body weights.

2.1.4. Body Mass Index and Its Use in Predicting Mortality and Morbidity in Asians

Although the evidence suggests that East Asians may be at a great risk of developing T2DM, this population has been largely overlooked in research. In part, a lack of investigation of weight-related health consequences in East Asians may be

a result of how overweight and obesity are defined. The NHLBI and WHO BMI cut-offs were developed based on morbidity and mortality rates attributable to increasing body fat content. In the first three columns of Table 1, the WHO weight classifications (also NHLBI) and the risk levels of body weight related comorbidities are presented. This increased risk between BMI and comorbidities was observed at BMI ≥25 kg/m^2 in Caucasian populations (NIH, 1998; Stevens & Nowicki, 2003). However, recently it has been argued that the application of the Caucasian specific threshold to multiethnic groups may be inappropriate. The current BMI cut-offs lose their predictive value among some ethnic groups, particularly among Asians. Recognition of increased body weight-related health problems among Asians has led to the development of separate Asian BMI classification WHO guidelines (WHO, 2000). These guidelines are presented in the fourth column of Table 1. The recommended BMI cut-offs for Asians have been lowered to match the risk of comorbidities associated with increasing body weight.

Table 1
BMI Classification (WHO, 1998) and Recommended BMI Cut-offs for Asians (Steering committee of the WHO Western Pacific Region, 2000)

Classification	WHO BMI Cut-off	Risk of Comorbidities	Asian BMI Cut-off
Normal Range	18.5-24.9 kg/m^2	Average	18.5-22.9 kg/m^2
Overweight	25-29.9 kg/m^2	Increased	23-24.9 kg/m^2
Obese I	30-34.9 kg/m^2	Moderate	25-29.9 kg/m^2
Obese II	35-39.9 kg/m^2	Severe	≥30 kg/m^2
Obese III	≥ 40 kg/m^2	Very Severe	

Several studies have supported the lower cut-offs in Asian populations. In the Behavioral Risk Factor Surveillance System (BRFSS) data, the age, gender, and BMI adjusted odds ratio for T2DM was 1.6 times higher in the Asian groups

compared to CA (McNeely & Boyko, 2004). In this study, the average BMI for Asian Americans was 24 kg/m^2 and 26.8 kg/m^2 for CA. The percentage of people who were overweight and obese was 32.8% and 4.8% for Asians, and 39.2% and 21.8% for CA, respectively. Although not as heavy, Asians were 60% more likely to develop T2DM than Caucasians. The unusual relationship between obesity and T2DM in Asians was captured, but because all individuals of Asian descent were grouped together as Asians, East Asian data alone were not available. Furthermore, most of the work related to obesity and T2DM have been conducted with South Asians (e.g., Indian) because of the excessive rate of type 2 diabetes in this population.

2.1.5. BMI and Body Fat Distribution in Asians: The Importance of Abdominal Fat Distribution

The increased comorbidities seen at lower BMI in Asians may be related to the differing relationship between BMI and percent body fat (Deurenberg, Deurenberg-Yap, & Guricci, 2002). Compared to Caucasians, various Asian groups have been found to have a higher percent body fat when matched for BMI (Deurenberg-Yap & Deurenberg, 2003; Gallagher et al., 2000; Gurrici, Hartriyanti, Hautvast, & Deurenberg, 1998; J. Wang et al., 1994). Although not visibly obese, East Asians may actually be *fatter* than Caucasians.

Different body shapes may partially explain the differences in BMI and body fat between Asians and Caucasians. Asians generally have shorter legs, longer torsos, and smaller body frames (Deurenberg et al., 2002; Deurenberg, Deurenberg Yap, Wang, Lin, & Schmidt, 1999; Deurenberg, Yap, & van Staveren, 1998; Gurrici,

Hartriyanti, Hautvast, & Deurenberg, 1999; Luke et al., 1997). Thus, for Asians, most of the height comes from the longer torso, and most of the weight comes from the torso area. Thus, Asians are more prone to develop an abdominal fat distribution. The BMI, which assumes comparable body compositions and frames, fails to detect anthropometric differences between ethnic groups.

The anthropometric differences that adversely affect health are closely related to the distribution of fat. Fat accumulation around the abdomen in comparison to the peripheral area has particular significance in the development of insulin resistance and T2DM (DiPietro, Katz, & Nadel, 1999; Okosun & Dever, 2002). Abdominal obesity, as assessed by waist to hip ratio (WHR) or waist circumference (WC), is associated with an increased risk for developing T2DM, independent of BMI (Carey et al., 1997). In the Nurses' Health Study, individuals with a large WHR (top 10%) had 3 times the risk of developing T2DM as compared to people with a small WHR (bottom 10%). Moreover, the risk of developing T2DM was 5 times greater in the large WC group (top 10%) compared to the small WC group (bottom 10%). Abdominal fat accumulation is important in the development of T2DM and Asians are prone to cumulate fat around the abdominal area because of physical characteristics. However, most of these findings come from research with South Asian populations.

2.1.6. Rationale for Studying East Asians

Asians in the U.S. are diverse in their ethnicity, culture, and language. To date, studies investigating ethnic differences in health status either have grouped Asians with Pacific Islanders (sometimes categorized as *Others*) or studied one

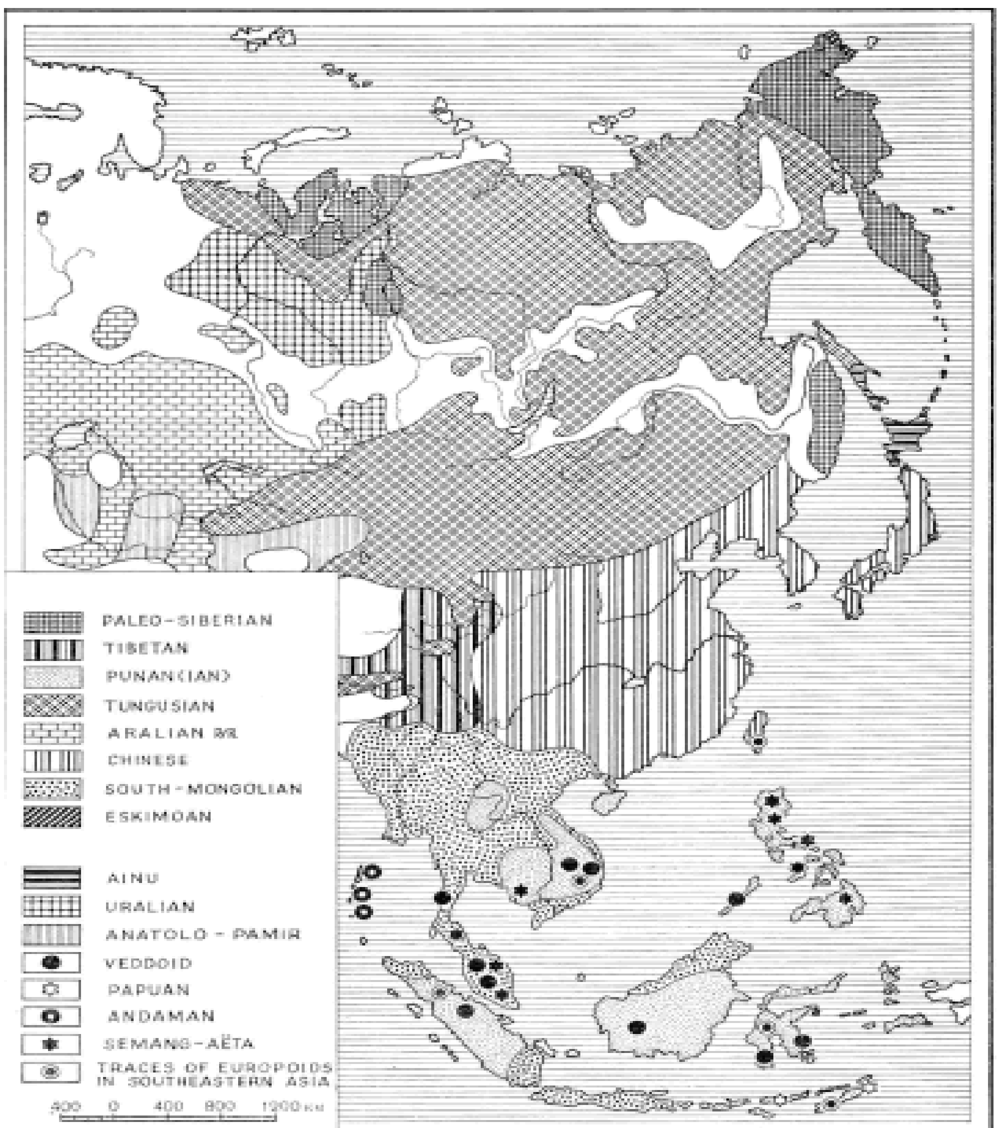
ethnic group from a single Asian country (mostly Asian Indians). The former method can lead to erroneous conclusions because Asian/Pacific Islanders are heterogeneous in genetic, cultural, and social backgrounds (Esperat, Inouye, Gonzalez, Owen, & Feng, 2004). However, the latter method may lack generalizability of findings to all Asian groups. In the current study, the East Asian individuals were used as a group because of a common biological background, cultural, and social aspects (J. Kim & Chan, 2004b; Levin & Michael, 1962; Reeves & Bennett, 2004). In the next section, the rationale for grouping Chinese, Korean, and Japanese, and investigating them as one group is provided.

Figure 1
Three Sub-groups of Asia: East Asia, South Asia, and Southeast

Ethnolinguistic background. Figure 1 shows three parts of Asia: East Asia, Southeast Asia, and South Asia (Levin & Michael, 1962). South Asians (e.g., India, Sri Lanka, Pakistan) are Indo-European in origin and have no direct genetic link to

East Asians. Southeast Asians are Malay and Polynesian in origin. Chinese, Korean, and Japanese are different from South and Southeast Asians in that East Asians are Mongoloids in their origin. East Asians share a geographical origin, and even today are grouped based on geography. In Figure 2, according to Biasutti's classification of East Asians, Chinese, Korean, and Japanese share a Chinese ethnic origin (Levin & Michael, 1962).

Figure 2
Races of Asia (Biasutti's Scheme of Northeast Asians)



Dietary culture. EA share cultural artifacts. Because of the geographical proximity, China had a direct impact on Korea. Since 250 B.C. Japan also shared the culture of Korea and China. The dietary culture spread with the advancement of agriculture of China. Along with rice cultivation, health beliefs associated with diet also spread through Korea and Japan, such as Yin and Yang theory (Ho & Lisowski, 1997; Yanchi, 1988). A balance between yin and yang dietary components is considered vital and deficiencies of either are believed to result in illness (Ho & Lisowski, 1997; Yanchi, 1988). Thus, daily diet is considered to be the most important aspect of medicine for health and illness in Chinese culture. Beliefs in Chinese medicine are commonly shared among Koreans and Japanese. Even today, Chinese, Korean, and Japanese adhere to this dietary belief, but it is not as frequently practiced in other parts of Asia (J. Kim & Chan, 2004b).

Migration history & experience in the U.S. East Asians in America share a similar migration history and experience in the U.S. Chinese, Japanese, and Koreans started migrating to the U.S. to be a cheap source of labor in the mid 1800's. As a cheap labor force in the U.S., East Asians shared racial discrimination and segregation from mainstream society. East Asians have shared the second half of U.S. history with other fellow Americans and also experienced their own lives of marginalized and discriminated immigrants (S. Chan, 1991).

Socioeconomic status & duration of residency in the U.S. Immigrants with longer duration of residency in the U.S. have more years of formal education and better jobs (Kandula & Lauderdale, 2005). Because East Asians share similar duration of residency in the U.S., they often share similar socio-economic

backgrounds (Reeves & Bennett, 2004). This is different from other Asian immigrants such as Southeast Asian, who are mostly refugees from Vietnam, Cambodia, Laos, and Hmong. More Southeast Asians live under the national poverty line and their household income is significantly lower than most other Asian groups and the national average (CDC, 2000).

East Asian communities in the Maryland & Virginia area. According to the U.S. Census 2000, various Asian groups comprised the second largest immigrant group in the U.S. Chinese, Koreans, and Japanese are the largest subgroups of Asians (Reeves & Bennett, 2004). East Asians comprise 42.1% of total Asians in the U.S. In the Maryland area, Chinese and Korean groups are the second and fourth largest foreign-born groups, respectively. In the Virginia area, Koreans and Chinese were the second and seventh largest foreign-born groups, respectively. For Koreans in the U.S., Montgomery County, MD is the 9^{th} most popular county and Annandale, VA is the 22^{nd} most popular city to reside.

In summary, because of the shared background in the ethnic and cultural aspects of East Asians, particularly the dietary culture, Chinese, Korean, and Japanese form an appropriate collective group for the current investigation. Their similar life experience and history in the U.S. further reduce the differences within this group. The longer duration of residency in the U.S. also allows examination of the influence of varying degrees of acculturation on health risk factors. Moreover, the number of East Asians in the greater Washington DC area is increasing. Thus, investigating the health in this population is essential to improve public health in this area.

In summary, East Asians may have a centralized distribution of body fat that has a negative health impact. Because BMI classifications do not capture the differences in body fat distribution in Asians, and the research in this area has not been conducted extensively with East Asians, the health consequences of body weight problems may have been underestimated in East Asians. In the proposed study, anthropometric measures were compared between East Asians and Caucasians to address the differing relationship of weight and metabolic measures in these two ethnic groups. For the purpose of comparing East Asians to Caucasians, the current study recruited two weight groups: BMI < 25 kg/m^2 (normal weight) and 25 ≤ BMI < 35 kg/m^2 (overweight and obese I). Thus, this part of the study had a 2 (ethnicity) x 2 (weight group) between subjects design.

2.2. Insulin Resistance

2.2.1. Function of Insulin and Defining Insulin Resistance

Insulin is a hormone responsible for the regulation of glucose, lipid, and protein metabolism. In a healthy person, increases in blood glucose concentrations in response to ingested food stimulate the pancreatic β-cells to secrete insulin. Insulin then facilitates glucose disposal in muscle tissues, thus allowing homeostasis to be achieved in the body. Insulin resistance is characterized by a lack of physiological response to insulin. Insulin resistance in muscle tissues, the inability of muscles to effectively respond to insulin, leads to gradually increasing blood glucose concentrations. Increasing blood glucose leads to progressively increasing

compensatory insulin production in the pancreas, and chronic overproduction of insulin by β-cells can lead to β-cell failure (Guyton & Hall, 2000). Thus, insulin resistance is one of the primary risk factors for developing T2DM (Lillioja et al., 1993). Unfortunately, by the time impaired glucose metabolism is detected by elevated fasting glucose concentrations or glucose tolerance test, significant proportion of β-cell destruction may have already occurred (Ferrannini, 1997). Thus, preventing T2DM will be more successful if earliest indication is detected while glucose responses are still intact. Therefore, investigating insulin responses/resistance is imperative in preventing T2DM development.

Defining insulin resistance is difficult. There is no clear guideline or cutoff for insulin resistance. The gold standard for diagnosing insulin resistance is euglycemic hyperinsulinemic clamp method. However, the clamp method is invasive and time consuming, thus a simple method to be used in a clinical setting for fasting insulin resistance was developed. The homeostasis model assessment (HOMA) of insulin resistance is calculated using the following formula: (fasting glucose (mmol/l) x fasting insulin (μIU/ml))/22.5. Increasing scores indicate higher resistance to insulin. No clear cutoff has been suggested, but in clinical practice, a HOMA-IR score of 2.5 or 3 is used to indicate insulin resistance in non-pregnant adults (Matthews et al., 1985). The validity of these cutoff values comes from comparison with the clamp method values.

2.2.2. Mechanisms Connecting Obesity and Insulin Resistance

*A*bdominal obesity and insulin resistance are two primary causal factors for the development of T2DM. Although mechanisms connecting obesity and insulin

resistance are not clearly understood, one of the most convincing mechanisms involves the action of free fatty acids and obesity precedes insulin resistance. Obese individuals have increased adipose tissue mass, resulting in elevated circulating free fatty acids, also known as non-esterified fatty acids (NEFAs). These NEFAs set off a pro-inflammatory cascade that result in enhanced production of tumor necrosis factor α (TNFα). TNFα suppresses the fatty acid oxidation rates. Suppressed rates of fatty acid oxidation in turn elevate circulating NEFAs and TNFα creating a vicious cycle, which would result in worsening of insulin resistance (G. R. Steinberg, 2007). Expression of TNFα is high in obese individuals, and elevated TNFα was related to reduced insulin stimulated glucose disposal (Hotamisligil, Shargill, & Siegelman, 1993). Furthermore, acute infusion of TNFα inhibited insulin stimulated glucose disposal (Plomgaard et al., 2005). Interestingly, the relationship between obesity and insulin resistance was pronounced in individuals with abdominal fat distributions.

Abdominal obesity also correlates with hypertension, high serum cholesterol, low HDL cholesterol, and hyperglycemia. Adipose tissue releases products that exacerbate these risk factors including: (1) Non-esterified fatty acids (NEFA), which overload muscle and liver with lipids, reduce their function and enhance insulin resistance; (2) Elevated pro-inflammatory cytokines such as C-reactive protein (CRP), which is commonly accompanied by obesity; and (3) An elevated plasma plasminogen activator inhibitor (PAI-1), which contributes to a pro-thrombotic state. (Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004; Juhan-Vague, Alessi, & Morange, 2000). In addition, insulin resistance enhances output of very low density

lipoprotein (LDL), and predisposes individuals to be glucose intolerant (hyperglycemia), which can lead to the development of T2DM. The obesity and insulin resistance are closely linked, and because they trigger cascades of hormone responses stated above, all these risk factors tend to occur together in individuals.

2.2.3. Insulin Resistance Syndrome

In 1988, the co-existence of these risk factors was first noted by Reaven, and a term “Syndrome X” was coined to refer to the aggregation of cardiovascular disease risk factors, which include insulin resistance/hyperinsulinemia, obesity, hyperglycemia, hypertension, hypertrigyceridemia, and reduced HDL cholesterol (Bjorntorp, 1991). The symptom cluster is defined as a syndrome because these risk factors tend to aggregate in individuals at greater than chance frequency and are more harmful than having a single factor (Isomaa et al., 2001; Lempiainen, Mykkanen, Pyorala, Laakso, & Kuusisto, 1999; Trevisan, Liu, Bahsas, & Menotti, 1998; Vanhala, Pitkajarvi, Kumpusalo, & Takala, 1998; Yip, Facchini, & Reaven, 1998). This cluster of health risk factors has gained significant attention not only because of cardiovascular disease associated consequences, but also the association with other diseases, such as T2DM and some cancers (Moore, Park, & Tsuda, 1998; Stoll, 1999).

Syndrome X was later renamed the “Insulin Resistance Syndrome” to underscore insulin resistance as the common denominator, which preceded other facets of the syndrome (Haffner et al., 1992). However, now it is commonly referred to as the Metabolic Syndrome (MS) because of disagreement regarding whether insulin resistance is the underlying factor for MS.

To introduce MS into clinical practice, clinical diagnostic criteria have been created by the WHO in 1998. Since then, several modifications were made to encourage the usage of the criteria in the clinical setting by simplifying the criteria. One of the most studied criteria is created by the National Cholesterol Education program (NCEP) Adult Treatment Panel III (ATP-III). The ATP-III guideline uses waist circumference as a surrogate of insulin resistance because insulin resistance test is not practical in clinical settings. According to guideline diagnostic criteria any 3 of following 5 conditions constitute diagnosis of metabolic syndrome: (1)Elevated waist circumference (≥ 102 in men and ≥ 88 in women); (2) Elevated triglycerides (≥ 150 mg/dl) or on drug treatment; (3) Reduced HDL-C (< 40 mg/dl in men and < 50 mg/dl in women or on drug treatment; (4) Elevated blood pressure (≥ 130 mmHg systolic BP or ≥ 85 mmHg diastolic BP or on drug treatment); and (5) Elevated fasting glucose (≥ 100 mg/dl or on drug treatment). Based on the ATP-III guideline diagnostic criteria, 22.8 and 22.6% of the U.S. men and women, and 4.6, 22.4, and 59.6% of normal-weight, overweight, and obese men, respectively, have MS (Y. W. Park et al., 2003).

On a global level, the prevalence rate of MS is rising, especially in East Asian regions. In Korea, the MS rate has increased and the total percentage of the population with MS has reached levels comparable to those of western countries (M. H. Kim, Kim, Choi, & Shin, 2004). Recently, it has been noted that MS in general, develops in East Asia with less visceral obesity than in Caucasians (Grandinetti, Chang, Theriault, & Mor, 2005; Nestel, 2004). The ATP-III criteria, thus modified its cut-offs to accommodate the interethnic differences in the relationship between risk

factors and the health outcomes: ≥ 90 cm in men and ≥ 80 cm in women for Asians (Grundy et al., 2005). This recommendation may have resulted from the recognition of differing body frame sizes between Asians and Caucasians, and further indicates the need to understand the relationship between weight status (different anthropometric measures) and metabolic responses and the subsequent development of chronic disease in East Asians. Therefore, in this study, the relationship between weight status, particularly abdominal obesity, and insulin was one of the major focuses of this investigation.

In summary, East Asians may have a unique relationship between body weight, central obesity, and its health consequences, yet the relationship is not clearly understood. East Asians are prone to develop central obesity, which may predispose them to be "metabolically obese" even at lower BMI. The problem of obesity and insulin resistance will only get worse as the number of East Asians increase in the U.S. and as they adopt a Western lifestyle. In the next section, two major characteristics of a Western lifestyle contributing to obesity and insulin resistance, high fat consumption and low physical activity, will be discussed in relation to T2DM development in East Asians.

2.3. Lifestyle Factors Affecting Obesity and Insulin Resistance: Diet and Physical Activity

Genetic factors may predetermine the course of health and disease, but the expression of the disease can be determined by lifestyle factors (Roberts & Barnard, 2005). Chronic diseases develop over a long period of time, usually involving the

entire lifetime (Roberts & Barnard, 2005). A dramatic increase in the T2DM rate in recent years is attributable to the environment and lifestyle changes because changes in the human genome over such a short period are highly unlikely (Booth, Gordon, Carlson, & Hamilton, 2000). Lifestyle factors, mainly a diet high in fat, particularly saturated fat, and physical inactivity, affect the development of obesity, insulin resistance, and subsequent T2DM (van Dam, 2003). For instance, Chinese sub-populations, who have similar genetic characteristics, have shown substantial variation in the prevalence of impaired glucose tolerance and T2DM attributable to differing lifestyle factors (Chang et al., 2000).

2.3.1. Acculturation and Its Relation to Lifestyle Changes in Immigrants

The rate of Asian immigration to the U.S. has increased markedly in recent years. Based on the 2000 U.S. Census, 5% of the U.S. population is Asian. The number of Asians will continue to grow as various Asian groups currently make up the second largest number of immigrants (31.2%) after Latino groups. Chinese, Koreans, and Japanese are the largest subgroups of Asians and consist of 42.1% of the total Asians in the U.S. (Reeves & Bennett, 2004). This increase in EA populations within the U.S. provides a unique opportunity to study the role of acculturation, lifestyle changes and resulting health outcomes among EA.

2.3.1.1. Definition of acculturation

Immigrants bring personal values, traditions, language, skills, and manners to the new countries to which they emigrate. When people migrate to a new country, the immigrants begin to learn and assimilate into mainstream society. This

“acculturation” is the process by which foreign-born individuals and their children acquire and accommodate the values, beliefs, language, and customs of the new country. Acculturation may include health behaviors such as dietary choices and physical activity patterns, which are known to impact health and disease outcome (Unger et al., 2000). Acculturation is not limited to instances when individuals move from one country to another, but also occurs when different sub-cultures co-exist within one country. However, for the purposes of this study, acculturation was defined by the change which occurs within a minority individual by assimilating to the new dominant culture.

2.3.1.2. Acculturation and increased risk of type 2 diabetes mellitus

Unfortunately, acculturation to the mainstream culture of the U.S. can have negative health consequences for some people when unhealthy behaviors, such as increased fat intake and reduced physical activity, are adopted (Lauderdale & Rathouz, 2000). Higher rates of chronic diseases seen in East Asians have been largely attributed to changes in dietary intake and decreased physical activities (Chang et al., 2000; Kawate et al., 1979; M. M. Lee et al., 1994; Manson & Spelsberg, 1994). For this reason, people from Asia who migrate to Westernized countries have a greater risk of developing T2DM than counterparts in their native countries (Manson & Spelsberg, 1994). Two decades ago, Kawate and colleagues demonstrated that Japanese living in Japan had a lower risk of developing T2DM compared to Japanese living in Hawaii. The increased risk for Japanese living in Hawaii was due to adoption of a Western lifestyle (Kawate et al., 1979). This

Japanese population started to acquire diseases prevalent in their new country of residence.

2.3.1.3. Operational definition of acculturation in East Asians

Researchers investigating acculturation and disease development commonly use the number of years of residency in the U.S. or generational status (e.g., 1st generation, 2nd generation) to represent the degree of acculturation (Goel, McCarthy, Phillips, & Wee, 2004; Mooteri, Petersen, Dagubati, & Pai, 2004; S. Y. Park, Murphy, Sharma, & Kolonel, 2005). It is assumed that the more years spent in the U.S., the more likely individuals are to adapt to the U.S. mainstream culture and lifestyle. Indeed, it has been shown that the duration of residency in the U.S. is associated with increased chronic disease development in immigrants (Mooteri et al., 2004). However, the interpretation of the relationship between the years of residency in the U.S. and the development of chronic disease is difficult and more complicated than this simple index might reflect. The number of years of residency does not provide an underlying basis for changes in lifestyle. In addition, it is possible that individuals can remain in cultural isolation with minimal contact to a Western lifestyle for a long period of time, and thus not be affected by the mainstream culture. In other words, the years an individual has spent in the U.S., does not equal to a person's level of acculturation.

Thus, in the present study, acculturation was defined by the scores obtained from the Suinn-Lew Asian Self-Identity Acculturation Scale (SL-ASIA scale) (Suinn, Richared-Figueroa, Lew, & Vigil, 1987), which includes components of language, self-identity, social choices, behaviors, attitude, generation, and geographic history.

This definition should capture multifaceted aspects of acculturation and its relationship with changes in lifestyle and the development of subsequent risk factors.

2.3.2. Dietary Characteristics in East Asians

2.3.2.1. Dietary fat intake in East Asians

Japanese who migrated to the U.S., had a significant increase in insulin levels and dietary fat consumption compared to Japanese in Hiroshima (Egusa et al., 2002; Nakanishi et al., 2004). Japanese Americans had a higher fat intake, especially of animal origin saturated fats than native Japanese. Though total caloric intake also appeared higher in Japanese Americans, the difference was not significant. Others have reported that Asian diet provides less total energy intake, and less total-, saturated-and trans-fat than the typical American diet (J. Kim & Chan, 2004a; Lv & Cason, 2004; Takata, Maskarinec, Franke, Nagata, & Shimizu, 2004; Zhou et al., 2003).

Within East Asian Americans, more acculturated East Asians eat more fat, meat, meat alternatives, snack foods, sweets (chocolate, candies), soft drinks, and fast-food than less acculturated East Asians (Lv & Cason, 2004; Satia et al., 2001). Compared to recent immigrants, more acculturated Korean and Japanese Americans consumed more American foods and more fat (J. Kim & Chan, 2004a; Takata et al., 2004). Beliefs about traditional foods also appear to change along with new dietary habits. With increased duration of residence, individuals consumed traditional foods less frequently. Those with more Western dietary habits did not believe that the traditional foods were healthier than Western foods (Satia-Abouta,

Patterson, Kristal, Teh, & Tu, 2002). These are powerful examples of acculturation and its influence on belief and behavior changes in EA immigrants.

2.3.2.2. Dietary fat consumption and type 2 diabetes mellitus: possible mechanism

High fat consumption, particularly saturated fat consumption, is associated with weight gain and increasing rate of T2DM (Haag & Dippenaar, 2005). One of the proposed mechanisms to explain how increased saturated fat consumption increases weight gain is through the regulation of food intake. Feeding and satiety centers are located in the dorsolateral and ventromedial hypothalamic areas, respectively. In mice, saturated fatty acid increased neuronal activity in the feeding center, while unsaturated fatty acid increased neuronal activity in the satiety center of the hypothalamus (H. Wang, Storlien, & Huang, 1999). Recently, a molecular connection was found linking the high-fat Western diet and the disruption of insulin production, which leads to the progression of T2DM. When mice were fed a high-fat diet, the activity of the enzyme GnT-4a, which enables β-cells in the pancreas to sense blood glucose levels and produce the appropriate amount of insulin, was reduced. This reduction in the GnT-4a enzyme leads to the development of T2DM (Ohtsubo et al., 2005). Thus, EA with a Western diet, which includes a high fat consumption, particularly saturated fat, would more likely be overweight/obese, insulin resistant, and have T2DM.

2.3.2.3. Type 2 diabetes mellitus in East Asians: β-cell function failure

A growing body of literature suggests that Japanese and Koreans have compromised pancreatic functions, which predispose them to develop T2DM (Fujimoto et al., 2000; Kuroe et al., 2003; Matsuoka, 2000; S. Park, Park, & Jang, 2005). The “thrifty phenotype hypothesis” explains that fetal and infant nutritional environment factors are the dominant causes of T2DM (Hales & Barker, 2001). Based on fetal nutrition, the fetus develops its organs in the order of importance. Brain development is always the priority and the development of the remaining organs, including β-cells, is secondary. Thus, organ developments may be compromised when the fetal nutrition is poor. Furthermore, a poor nutritional environment signals the fetus that β-cell mass development is not important because the environment where it will be raised will not require massive production of insulin. As such, the nutritional environment is communicated to the fetus. However, if the fetus is born into the nutrition rich environment, and thus weight gain and insulin resistance occur, then the lack of β-cell mass proliferation may lead to premature development of T2DM. Specific evidence of dietary changes and its impact on T2DM development can be found in an animal study.

Animal data suggest that changes in the macronutrient composition of meals from an Eastern- to a Western-style diet may negatively impact β-cell function and insulin resistance (S. Park et al., 2005). Rats were fed either an Asian-style diet (AD; high carbohydrate, low fat, and protein source from grains) or a Western-style diet (WD; high in fat and protein source from animal). After 12 weeks, half of the AD animals were switched to a WD (AD-WD), and half of the WD animals switched to

AD (WD-AD). The remainder continued eating the original diet. The AD-WD rats showed an increase in plasma glucose and insulin, and displayed reduced compensation for the increased dietary fat. Park and colleagues speculated that during early stages of development the AD did not allow β-cell growth in young rats, and consequently these rats were unable to meet the increased insulin demand caused by changing to the WD. This lack of β-cell proliferation was further documented when the animals were sacrificed.

It is possible that the large increase in T2DM prevalence among East Asians is related to shifts in fat intake. The reserve capacity for additional insulin secretion may be insufficient to compensate for the increased insulin resistance due to an initial Asian diet in East Asians (Fujimoto et al., 2000; Kuroe et al., 2003; Matsuoka, 2000; S. Park et al., 2005). For East Asian individuals, high fat diet and body weight gain would have a severe impact on insulin and glucose responses, and in turn developing T2DM. In the proposed study, detailed information regarding dietary intake was assessed by using a computerized dietary intake record and its role as a mediating factor between acculturation and metabolic responses was examined.

2.3.3. Physical Activity among East Asians

Physical activity is another behavioral factor that can influence obesity and insulin resistance. Physical activity is a bodily movement resulting in energy expenditure while exercise is defined as a type of physical activity which is planned, structured, and repetitive, and performed to improve or maintain one or more components of physical fitness (ACSM, 2006). Sedentary activity, such as television viewing, is associated with an increased relative risk of developing T2DM for both

men and women (Hu, 2003; Hu, Leitzmann et al., 2001). This relationship held true, even after accounting for the level of inactivity. Conversely, increased physical activity and exercise reduce the development of insulin resistance and T2DM. For example, trained endurance athletes demonstrate significantly lower insulin levels in the fasting and postprandial state, and lower insulin resistance compared to their sedentary counterparts (Ebeling et al., 1993; Nuutila et al., 1994; Richter, Turcotte, Hespel, & Kiens, 1992). Japanese patients with T2DM and Chinese individuals with impaired glucose tolerant benefited from exercise interventions to increase muscle insulin mediated glucose uptake and reduce the rate of developing T2DM, respectively (X. R. Pan et al., 1997; Tamura et al., 2005). The positive effect of increased physical activity and exercise on health is evident, but the physical activity level in Asians is still very low.

Higher percentages of Asian Americans do not meet the current recommendation for regular leisure time physical activity compared to non-Asian Americans (Bolen, Rhodes, Powell-Griner, Bland, & Holtzman, 2000). Findings from the 1997 BRFSS show that Asian American men and women are twice as likely to be physically inactive then the U.S. born non-Asians. Furthermore, within Asian populations, leisure time physical activity (LTPA) was higher for the U.S. born Asians than foreign-born Asian Americans, and the likelihood of meeting recommended LTPA increased as years in the U.S. increased. However, the non-leisure time physical activity (NLTPA) was higher among non-U.S. born Asian Americans (Kandula & Lauderdale, 2005).

Higher NLTPA in recent immigrants and higher LTPA in acculturated Asians may be related to differences in socio-economic status of these two Asian groups. That is, more acculturated Asians have more education and better jobs, which are related to English proficiency and familiarity with the U.S. system, whereas more recent immigrants do not possess such skills. More recent immigrants will have laborious jobs and may have different means of transportation, other than driving; such activities may account for increased NLTPA. Additionally, many Asians believe that LTPA is an activity of luxury (time and money). Thus, Asians with higher socio-economical status (SES), who are often more acculturated, can afford LTPA. However, whether the acculturation is associated with changes in physical activity, which in turn leads to obesity and insulin resistance has not been demonstrated in East Asians.

2.3.3.1. Exercise and type 2 diabetes mellitus

Exercise increases the insulin-mediated glucose disposal in muscle tissues (Annuzzi, Riccardi, Capaldo, & Kaijser, 1991). Daily walking for >30 min is associated with a 20 to 45% risk reduction of T2DM (Hu, Leitzmann et al., 2001; Hu, Li, Colditz, Willett, & Manson, 2003; Hu et al., 1999; G. Hu et al., 2003; Wannamethee, Shaper, & Alberti, 2000; Weinstein et al., 2004). A fast walking pace was a significant predictor for a reduced risk of T2DM, independent of the walking time (Hu, Leitzmann et al., 2001; Hu et al., 1999; Wannamethee et al., 2000). Endurance exercise training enhanced insulin-mediated glucose disposal even in healthy individuals and has also been found to be effective in reducing MS (Henriksen, 2002; Irwin et al., 2002).

There are immediate effects of exercise as well as long term effects. For instance, an aerobic exercise of 37 minutes reduced glucose and insulin levels starting at the end of the observational period (approximately at 2h) (Bergfors, Barnekow-Bergkvist, Kalezic, Lyskov, & Eriksson, 2005). Furthermore, acute exercise improved insulin stimulated glucose disposal in the obese subjects 12h after the exercise (Devlin & Horton, 1985). The increase in total glucose disposal was also observed in the lean subjects although it did not reach statistical significance. The effect of exercise on the enhanced glucose uptake is seen in both obese and normal weight individuals, but the magnitude of improvement is greater in obese and in those who are already insulin resistant.

2.3.3.2. Exercise/high physical activity reduces insulin resistance: possible mechanisms

The molecular basis underlying the beneficial effects of exercise in the insulin resistance is still unclear, however, exercise seems to improve insulin resistance by improving muscle oxidation, decreasing muscle lipid, and increasing whole body rates of fatty acid oxidation (Bruce & Hawley, 2004). The mechanism by which exercise is effective in reducing insulin resistance may be mediated by weight loss, but even in the absence of substantial weight loss, increased physical activity has been shown to reduce the risk of T2DM (Tuomilehto et al., 2001).

In order for glucose to be metabolized in the body, it has to be delivered to the muscle, transported across membrane (to intracellular space) and then, phosphorylated to glucose 6-phosphate (Wasserman & Ayala, 2005). Movement of glucose from the blood stream into cells in the body is determined by muscle blood

flow, capillary recruitment, and endothelial permeability to glucose (Wasserman & Ayala, 2005). The number and activity of membrane glucose transporters determine the capacity for transporting glucose from interstitial to intracellular space. Finally, phosphorylation is determined by the amount of muscle hexokinase and hexokinase compartmentalization within the cell. Muscle glucose intolerance is a result of an alteration in one or more of these steps.

Skeletal muscle is a major consumer of glucose during exercise (Wasserman & Ayala, 2005). Both exercise and insulin stimulation increase capillary recruitment, and increase the surface area for diffusion of blood and decrease diffusion distance to muscles (Clark et al., 2003; Rattigan, Clark, & Barrett, 1997; Vincent, Barrett, Lindner, Clark, & Rattigan, 2003; Vincent et al., 2002). Although both exercise and insulin increase blood flow and capillary recruitment, the increase in muscle perfusion for a given increase in muscle glucose uptake is much greater with exercise (Laughlin, Korthuis, Duncker, & Bache, 1996). In insulin resistant individuals, impairment in insulin-stimulated muscle blood flow is evident (Laakso, Edelman, Brechtel, & Baron, 1992; H. O. Steinberg & Baron, 2002). Thus, hyperemia that occurs during exercise to increase delivery of glucose and other nutrients to muscles, may be an effective way to transport glucose for the people with compromised insulin mediated glucose uptake. In addition, exercise and insulin stimulation both increase the capacity for glucose phosphorylation (Wasserman & Ayala, 2005). In insulin resistant individuals, skeletal muscle hexokinase activity was reduced, but exercise can increase the capacity for glucose phosphorylation (Braithwaite, Palazuk, Colca, Edwards, & Hofmann, 1995; Vestergaard et al., 1995).

Although contribution of each component for reduced muscle glucose uptake is unclear, any condition that causes insulin resistance, involves a functional limitation in one or more of these components, and exercise seems to improve these functions.

In summary, there is evidence that lack of physical activity and diets high in fat are associated with development of obesity and insulin resistance. Also, East Asians who migrate to the U.S. may have an increased risk of developing T2DM. This consequence is most likely due to acculturation to the lifestyle in the U.S., which includes increasing dietary fat consumption and lowering physical activity. However, the effect of acculturation on health behaviors, subsequent weight gain, and insulin resistance has not been extensively examined.

2.3.3.3. Provocation of the current study

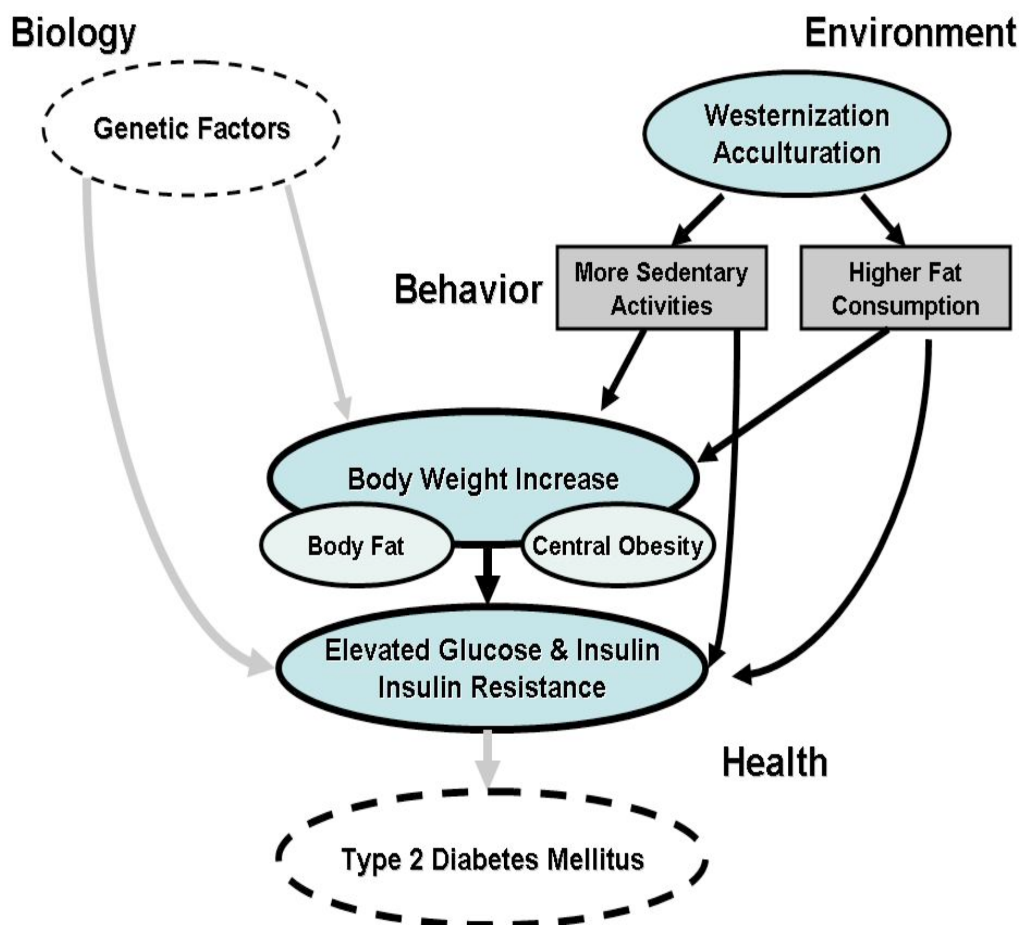
To date, most studies investigating insulin response in Asians have included South Asians and have used a glucose tolerance test. In a study by Cruz and colleagues in 2001, the investigators used a high fat meal instead of glucose to examine the postprandial glucose, insulin and triglycerides in South Asians in the United Kingdom. The meal was composed of 52% fat, 40% carbohydrates, and 8% protein. In the study, it was reported that in spite of comparable anthropometric measures and fasting metabolic profiles, postprandial glucose and insulin responses were higher in South Asians compared to Caucasians. This difference could not be explained by postprandial plasma lipid concentrations (Cruz, Evans, & Frayn, 2001). However, this study examined South Asians, whose BMIs were all below 27 kg/m^2, and the meal was designed to elicit a high fat response. In another study by

Dickinson and colleagues in 2002, investigators examined Chinese individuals' fasting and postprandial glucose and insulin responses. However, the investigators used white bread to elicit the glucose response, which is similar to the oral glucose tolerance test. Although 75-100g of a glucose meal is adequate to elicit insulin responses, this nutrient composition is not realistic. These meal tests do not represent a realistic macronutrient composition, and thus do not allow us to examine metabolic consequences due to regular meal consumptions. Furthermore, this study included only normal weight Chinese individuals. Therefore, in the current study, a naturalistic meal that met USDA dietary recommendations for 2,000 calories/day daily was used to elicit metabolic responses. Additionally, a larger number of participants, including an overweight group was recruited for the current study. One of the weaknesses of these previous studies was that the interaction term was not examined because the study design did not allow the interaction term to surface. In the current study, two different weight groups (normal weight and overweight) were recruited, and the interaction between ethnicity (East Asians and Caucasians) and weight categories on anthropometric and metabolic measures were examined.

The purpose of this study is to examine (1) the unique relationship between obesity and metabolic responses (at fasting and postprandial) in East Asians in comparison to Caucasians, and (2) the effect of acculturation on diet and physical activity pattern and its contribution to the development of obesity and insulin resistance in East Asians. Figure 2 represents a model of the conceptual framework of the proposed study. Both biological and environmental factors may contribute to the development of insulin resistance and subsequent T2DM in East Asians in the

U.S. In part, development of insulin resistance is dependent upon acculturation to a Western lifestyle, which is characterized by a high fat diet and low physical activity. These lifestyle factors contribute to increases in body weight, and consequent metabolic responses. Biologically, East Asians have a tendency to develop centralized body fat distribution and insulin resistance without apparent obesity. The physical features of East Asians allow them to accumulate fat in the abdominal area. Thus, as the model indicates, this progression can lead to the development of T2DM in East Asians more frequently than in Caucasians.

Figure 3
Biological and Environmental Determinants of Obesity and Insulin Resistance: Influence of Acculturation in East Asians Populations



3. Specific Aims and Hypotheses

The central hypothesis of the study was that East Asians would have a predisposition to develop insulin resistance and, therefore, insulin responses at fasting state and after a meal would be greater than in their BMI comparable Caucasian counterparts. Obesity, particularly central obesity, is associated with insulin resistance. Physical activity/exercise are associated with reduced insulin resistance (Bergfors et al., 2005; Bruce & Hawley, 2004; Devlin & Horton, 1985), whereas increased total energy and fat intake increases insulin resistance (Chang et al., 2000; Egusa et al., 2002; Kawate et al., 1979; M. M. Lee et al., 1994; Manson & Spelsberg, 1994; Nakanishi et al., 2004; Sun & Chen, 1994). An increased level of acculturation in East Asians was expected to be related to an increased consumption of high fat diets and reduced physical activity. Consequently, acculturated individuals were expected to be more overweight and have higher insulin levels, which result from adaptation to a Western lifestyle.

Differences in glucose and insulin responses to a standardized meal have not been examined in the East Asian population. Such differences in glucose and insulin responses may be important in understanding the metabolic consequences of daily meal ingestion. Characterizing changes in diet and physical activity that occur with acculturation to Western culture is also important. This information may lead to the development of dietary and physical activity recommendations suitable for each generation of East Asians. Results from this study may help target specific populations who are at increased risk of developing insulin resistance. Three aims were addressed as part of the proposed project in order to examine the relationship

between obesity, metabolic functions, acculturation, and ethnicity. The specific aims along with hypotheses are described below.

3.1. Specific Aim 1

Determine the relationship of anthropometric measures (WHR, WC, and body fat) and metabolic measures (glucose, insulin, and insulin resistance) as a function of weight status in East Asians in comparison to Caucasians. Studies to date have shown differences in anthropometric measures between East Asian and Caucasian populations, but their linkage to insulin and glucose concentrations have yielded mixed findings. This aim was addressed by examining glucose, insulin, and insulin resistance at fasting state in relation to anthropometric measures including percent body fat, waist-circumference, and waist-to-hip ratio in normal weight and overweight (based on NHLBI BMI cutoffs) East Asian and Caucasian groups.

Hypothesis 1a. *East Asians would have more centrally distributed body fat (waist-circumference and waist-to-hip-ratio) and a greater percent body fat compared to BMI matched Caucasians.*

Rationale: BMI measures are based on the assumption that individuals have similar body shapes, frames, and compositions. Because East Asians have a smaller body frame size and a longer torso area, their body weight relies heavily on tissues other than bone and connective tissues (Deurenberg et al., 2002; Deurenberg et al., 1999; Deurenberg et al., 1998; Gurrici et al., 1999; Luke et al., 1997). Thus, compared to BMI matched Caucasians, East Asians would have a

higher percent body fat, and a more centralized fat distribution (larger waist circumference and higher WHR). The overweight group would have a higher percent body fat, and a more centralized fat distribution compared to the normal weight group regardless of ethnicity.

Hypothesis 1b. *East Asians would have higher plasma concentrations of glucose and insulin when fasting relative to BMI matched Caucasians.*

Hypothesis 1c. *East Asians would be more insulin resistant relative to BMI matched Caucasians.*

Rationale: Research to date has shown that East Asian populations have a genetic predisposition to develop insulin resistance, and that the consequences of increasing body weight are more severe in East Asians than Caucasians in terms of developing insulin resistance and T2MD (Abate & Chandalia, 2001; Jia et al., 2002; McNeely et al., 2001; Nestel, 2004). Fasting plasma glucose and insulin, and insulin resistance would be higher in East Asians than Caucasians for both normal weight and overweight groups. The overweight group would have higher levels of fasting glucose and insulin, and be more insulin resistant than the normal weight group.

3.2. Specific Aim 2

Determine the extent to which postprandial glucose and insulin concentrations differ in response to a liquid meal as a function of weight status in East Asians in comparison to Caucasians. Postprandial hyperglycemia is an important risk factor for reducing the β-cell response and impairing insulin mediated glucose transport (Harris, Klein, Welborn, & Knuiman, 1992). During

glucose tolerance tests, Asian groups exhibited more unfavorable postprandial metabolic responses compared to Caucasians (Dickinson, Colagiuri, Faramus, Petocz, & Brand-Miller, 2002). However, postprandial glucose and insulin responses after a standardized meal with a more naturalistic macronutrient composition have not been examined. This aim was addressed by examining postprandial glucose and insulin concentrations after a standardized 16 oz liquid meal (Ensure Plus) as a function of ethnicity and weight status. Metabolic responses after a meal were also examined as summary scores: peak and area under the curve (AUC) of glucose and insulin.

Hypothesis 2a. *Postprandial glucose levels would be higher in East Asians compared to BMI matched Caucasians.*

Hypothesis 2b. *Postprandial insulin levels would be higher in East Asians compared to BMI matched Caucasians.*

Rationale: Because the literature to date suggests a greater predisposition for insulin resistance in East Asian populations, it was hypothesized that postprandial glucose and insulin concentrations would be higher in East Asians for both weight groups. In addition, the overweight group would have higher postprandial glucose and insulin responses compared to the normal weight group, regardless of their ethnicity.

3.3. Specific Aim 3

Examine the extent to which acculturation to a Western lifestyle affects physical activity patterns, dietary habits, obesity, and metabolic responses in

East Asians. This aim was addressed by using an acculturation scale, a 3-day food diary, a physical activity record, obesity measures, and postprandial insulin and glucose measures. Anthropometric measures, eating and activity habits, and metabolic responses would be examined in East Asians by varying level of acculturation.

Hypothesis 3a. *Increasing levels of acculturation would be positively correlated with high fat consumption and negatively associated with high physical activity.*

Hypothesis 3b. *Dietary and physical activity patterns would mediate the relationship between acculturation, obesity, and consequent poor metabolic responses in East Asians.*

Rationale: Because low physical activity patterns and high fat consumption are associated with the Western lifestyle, more acculturated individuals would have a higher BMI, greater percent body fat, and larger waist circumferences than less acculturated East Asians. Furthermore, a sedentary lifestyle and a high fat diet contribute to increased insulin resistance. Such a lifestyle could also predispose individuals to become overweight, which can exacerbate insulin resistance. Dietary and physical activity patterns are likely to mediate the association between acculturation and abdominal obesity and poor metabolic responses in East Asians. Therefore, a Western environment would be reflected in a higher glucose and insulin responses as a function of acculturation in East Asian individuals.

4. Methods

4.1. Study Design Overview

There were two parts of the study: (1) one laboratory visit for all participants and (2) a three-day dietary and physical activity monitoring for East Asians only. All qualified East Asian and Caucasian participants were invited for a laboratory visit, and these data were used to address Aims 1 and 2. East Asian participants kept a 3-day dietary and physical activity recording, and these data were used to examine Aim 3.

4.2. Participants

4.2.1. Recruited East Asian and Caucasian Participants

Thirty seven East Asian and 18 Caucasian individuals participated in the study. All East Asian participants identified both sets of his/her grandparents to be of East Asian descendents during a phone screen interview. Caucasian participants identified themselves as well as the maternal and paternal grandparents as European descent non Hispanic Whites. Participants were recruited via local newspapers, internet advertisement, from local universities, churches, and the surrounding metropolitan area for a study of body weight and insulin response.

4.2.2. Caucasian Participants from Existing Data Set

Twenty two Caucasian cases were selected from an ongoing study (PI: Dr. Patricia A. Deuster, Protocol#: G191BH). The larger ongoing study examines the physical and psychological correlates of obesity. The purpose of this ongoing study

is to examine the relationship between insulin resistance and the function of hypothalamic-pituitary-adrenal (HPA) axis by ethnicity (African American and Caucasian Americans) and obesity (obese and non-obese). Particularly, the study examines the HPA axis dysregulation as a possible mechanism to explain the interethnic differences in obesity and insulin resistance between African Americans and Caucasians. The data was collected at the Human Performance Laboratory over the past 3 years. The ongoing research utilizes a similar inclusion and exclusion criteria, and involves 4 visits with 3 different drug conditions. The data from the first visit, which is the baseline visit, were used for the current study. Caucasians were comparable to East Asians in BMI, gender, and age. Additionally, all Caucasian participants met the inclusion and exclusion criteria of the current investigation. This data set was free of any identifiable variables, thus being completely de-identified. No access to the code was provided to the investigator of this study.

4.2.3. Inclusion and Exclusion Criteria

Participants were healthy men and women between the ages of 18 and 50 years, and between the BMI of 18 and 35 kg/m^2. Children and individuals over the age of 50 were excluded from the study because of increased insulin resistance and different endocrine responses to a standardized meal (Arslanian & Kalhan, 1994; Kuroe et al., 2003; Nakanishi et al., 2004). Participants with one or more of the following conditions were excluded from the study: (1) Conditions that affect metabolic responses: pregnancy, insulin/drug dependent and independent diabetes mellitus, liver disease, and pancreatic diseases; (2) Diagnosed heart disease

because heart disease has a high comorbidity with obesity and T2DM; (3) Use of beta adrenergic blockers, glucose-lowering agents, steroids, growth hormone, or any other medications known to affect metabolic responses; (4) Active suicidal ideation or otherwise in need of immediate treatment and/or on chronic use of psychoactive medications, such as the use of antidepressants; (5) Menopausal because of different metabolic responses; and (6) Insufficient ability to understand English.

4.3. Procedure

4.3.1. Phone Screen

Each participant was phone-screened (See Appendix 2 for Phone Screen Script and Form). All participants had to meet inclusion and exclusion criteria during a phone screen. Qualified participants were invited to the Human Performance Laboratory for a 3-hour morning visit between 7 and 8 a.m. All female participants' laboratory visits were scheduled during follicular phase of their menstrual cycle: between the 4th and 10th day after the start of a period. Even though some studies have shown no relationship between glucose metabolism and menstrual cycle (Toth, Suthijumroon, Crockford, & Ryan, 1987; Yki-Jarvinen, 1984), all female participants completed their laboratory visit during follicular phase in order to reduce any variability in glucose metabolism associated with the cycle (Diamond, Simonson, & DeFronzo, 1989; Marsden, Murdoch, & Taylor, 1996). The day before the visit, a reminder call was placed. Participants were asked to abstain from eating after midnight, and caffeine, alcohol, tobacco, and strenuous exercise for at least 12

hours before the test period. In addition, participants were instructed to drink at least 64 ounces of water over the course of the day before the visit to increase the accuracy of the body composition measure.

4.3.2. Laboratory Visit

Laboratory visit portion of the study was conducted in the Human Performance Laboratory (HPL) (supervised by Patricia A. Deuster, Ph.D.) at the Uniformed Services University of the Health Sciences (USUHS, Bethesda, MD). Once informed consent was obtained, height, weight, and body fat percent measures were obtained (See Appendix 4 for a copy of informed consent document). Upon completion of anthropometric measures, a trained technician (Nicole Fendrick or Stacey Zeno) inserted indwelling catheters for blood drawing in an antecubital vein of the forearm. As soon as the catheter was inserted, a fasting glucose level was tested. Any participant with a fasting blood glucose ≥ 126 mg/dl were excluded from participating in the study because not meeting this cut-off may indicate undiagnosed T2DM or food consumption prior to the visit. Figure 4a and 4b show visual description of the laboratory visit timeline and ambulatory monitoring timeline. In the following section, procedures regarding anthropometric measures, a liquid meal test, and self-report questionnaires are described.

Figure 4a
Laboratory Visit Timeline for both Caucasians and East Asians

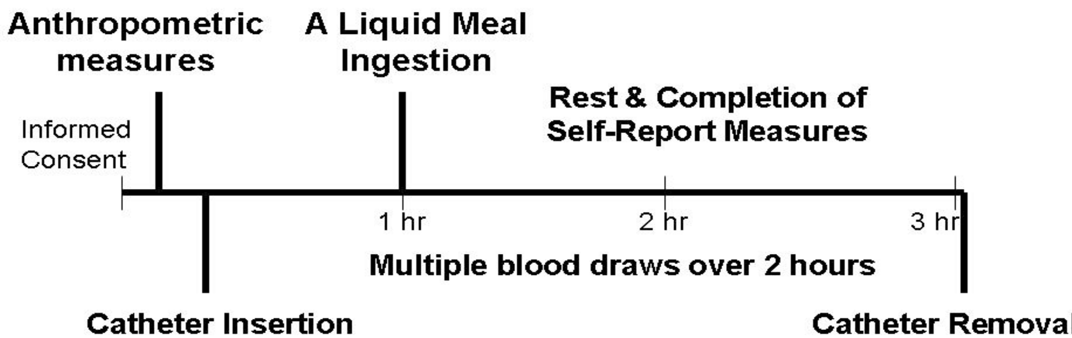
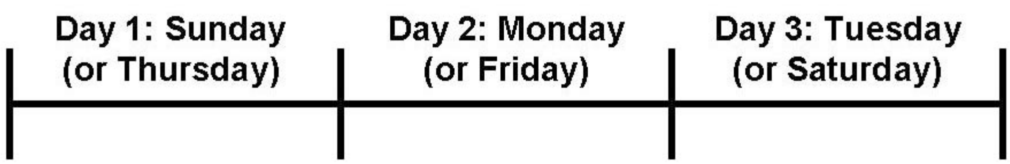


Figure 4b
Three-day Dietary and Physical Activity Monitoring Timeline for East Asians Following the Laboratory Visit



Note: Each participant had either a Sunday to Tuesday monitoring period or a Thursday to Saturday monitoring period.

4.3.2.1. Anthropometric measures

Body weight was measured with a calibrated balance beam metric scale to the nearest 0.1 kg, and height was measured to the nearest 0.1 cm while the participant was wearing light clothing and no shoes. BMI was calculated from height and weight. Percent body fat was estimated by bioelectric impedance (BEI) with the portable RJL body composition analyzer (RJL Systems, 1992). Waist and hip circumferences were measured with an inelastic tape around the waist and hip using standard techniques (ACSM, 2006). Waist to hip ratio was computed by using the

waist and hip measurements. Waist circumference and waist to hip ratio were used as the measures of central obesity.

4.3.2.2. Liquid meal test

A liquid meal was used to examine glucose and insulin responses. Each participant drank 2 cans of Ensure-Plus (16 oz). The changes in plasma glucose and insulin were monitored at 10, 30, 50, 70, 90, and 120 minutes following the meal ingestion. 16 oz. of Ensure Plus provides 720 kcal comprised of 56.4% carbohydrates, 29% fat, and 14.6% protein. The rationale for selecting two cans of Ensure Plus was to simulate a caloric intake (approximately 700 kcal/meal) similar to a realistic meal based on a 2,000 kcal/day diet for adults. Ensure is available in several flavors (vanilla, chocolate, strawberry, and butter pecan), is gluten and lactose-free, kosher, and is low in cholesterol. This liquid meal has been used previously in other studies and is known to stimulate both glucose and insulin responses (French et al., 1990; Goetz, French, Thomas, Gingerich, & Clements, 1995).

4.3.3. Self-report Measures

During the 2-hour postprandial glucose and insulin monitoring period, participants completed a Demographics form, and questionnaires on acculturation and stress. East Asian participants completed all questionnaires. Caucasian participants completed the Demographic Questionnaire and the Stress Profile. Copies of each questionnaire are provided in Appendix 3.

The Demographic Questionnaire includes questions on age, gender, date/place of birth, ethnicity/race, level of education, annual household income, and employment information. Socio-economic status may be associated with health outcomes. Thus, education and income status were measured as a proxy of socio-economic status.

The Suinn-Lew Asian Self-Identity Acculturation Scale (SL-ASIA scale) is a 26-item questionnaire used to assess acculturation for Asian American populations (Suinn et al., 1987). It was adapted from an acculturation rating scale for Mexican Americans and has been applied to Asian Americans. It has Language, Identity, Social Group, Behaviors, Generation and Geographic History, and Attitude subscales. The questionnaire was validated with college student samples. The summary scores of the scale were significantly associated with generation level, place of upbringing, and self-rating of identity (Suinn et al., 1987). The questionnaire uses a likert scale with each item ranging from 1 to 5: A low score reflects low acculturation to the U.S. culture while a high score reflects high acculturation to the U.S. culture. The total scores from the AL-ASIA scale were used to represent the level of acculturation in Aim 3. The internal consistency Cronbach's α ranged from 0.88 to 0.91 (Suinn, Ahuna, & Khoo, 1992; Suinn et al., 1987). This questionnaire was given only to East Asian participants.

Stress may be relevant to obesity and insulin resistance because chronic stress appears to promote the development of obesity and elevated levels of insulin via elevated stress hormones (i.e., ACTH, cortisol) (Bjorntorp, 2001; Bjorntorp & Rosmond, 2000). Additionally, a close relationship has been found between

acculturation and self-reported stress (Uppaluri, Schumm, & Lauderdale, 2001). Thus, general levels of stress and acculturative stress (only for East Asians) were examined by using two different questionnaires.

The Stress Profile (SP) (Nowack, 1999) was used to quantify life stress. The SP has 123 items that provide scores in 15 areas related to perceived stress and health risk, with measures for response bias and inconsistency. It assesses stress vulnerability and resistance across several domains to include Perceived Stress, Health Habits (Diet, Sleep, Exercise, Preventive), Social Support, Type A Behavior, Cognitive Hardiness, and Coping Style, and predicts risk for stress-related psychological and physical illness. Scores on the SP can be used to examine the differences among groups in levels of life stress. The SP has adequate internal consistency (α= 0.72~ 0.91) and reliability (r = 0.76~0.86). The SP was validated on an ethnically-diverse adult population (Nowack, 1999).

Acculturative Stress Scale (AS) is a 36-item likert scale, originally designed to assess acculturative stress levels among international college students (Sandhu & Asrabadi, 1994). It has six principal factors: Perceived Discrimination, Homesickness, Perceived Hate, Fear, Stress due to Change/Culture Shock, Guilt, and nonspecific items. The AS was used to examine additional stress related to feelings of being a "foreigner" in the U.S. regardless of generation status. High scores on this questionnaire reflect more acculturative stress. Items have face validity in assessing stress associated with acculturation. This questionnaire was given only to East Asian participants.

4.3.4. Three-Day Dietary Intake and Physical Activity Monitoring

Dietary intake and physical activity were assessed only in East Asian participants because the purpose of Aim 3 was to understand the effect of acculturation to a Western lifestyle in East Asians. Participants were instructed to record dietary intake and monitor physical activity for 3 consecutive days including one weekend day and two week days (see Figure 4b). Information from a 3-day dietary and physical activity recording was used to generate dietary fat intake and physical activity scores for Aim 3.

4.3.4.1. Dietary intake report

Participants received instructions on how to properly record dietary intake using a Palm m100. The participants used 9 lbs capacity portable scale to measure all foods and record the weight (Sbrocco et al., 2005). The Palm Pilot contains a 2 megabyte internal disk for recording dietary intake. The program contains an expandable database of 1,500 everyday foods and their nutrient contents. If a food item was not found from the list, participants were instructed to find a closest substitute item to enter into the Palm. Participants were asked not to alter their eating habits during this 3 day period. The average percent dietary fat intakes over 3 days were used to represent the Western diet in Aim 3.

4.3.4.2. Physical activity monitoring

In order to monitor physical activity, participants wore an Actiheart-accelerometer, and also completed *the Bouchard Three-Day Physical Activity Record*. Participants wore the Actiheart by Mini Miter (Mini Mitter Co., Inc., 2004) on

the same 3-days that they were recording dietary intake. The *Actiheart* is an innovative device that records physical activity and heart rate with a high level of accuracy (Brage, Brage, Ekelund et al., 2005; Brage, Brage, Franks, Ekelund, & Wareham, 2005). It weighs 10 grams and is placed on the left chest with adhesive electrodes. Actiheart includes both an omnidirectional accelerometer and an ECG signal processor. Using data from the Actiheart, average daily total energy expenditure throughout the 3-day monitoring period were obtained. Percent time spent engaged in high intensity physical activity was also measured.

Actiheart is advantageous over other commonly used methods of measuring physical activity, such as a pedometer and a wrist watch activity monitoring device. For instance, a pedometer does not allow a distinction between walking and running, thus the intensity of the physical activity is not measured. Additionally, a pedometer cannot detect upper body movements; therefore, it may not yield accurate estimates of total physical activity. Similarly, a wrist watch activity monitoring device cannot detect lower body movements, therefore, activities such as cycling would not be taken into consideration. Further, depending on where the placement of a watch (dominant vs. non-dominant hand), the activity level can be over- or under-estimated.

The *Bouchard Three-Day Physical Activity Record (TPAR)* was used to assess daily activity including leisure, non-leisure, and occupational activity (Bouchard et al., 1983). The TPAR was used to self-record daily physical activities over 3 days. Participants recorded their activity in 15 minute intervals. The TPAR

has test- retest interclass correlations of r = 0.97 with 6-10 day records (Bouchard et al., 1983).

4.3.4.3. Follow-up visit

East Asian participants returned to the USUHS approximately a week after their laboratory visit. During this time, the Palm Pilot, the Actiheart, and the activity recording were collected and reviewed for completeness. If a participant did not complete the dietary and physical activity monitoring records, they were given another chance to complete 3-day monitoring of diet and physical activity.

Caucasian participants did not have the follow-up visit to the laboratory because Caucasian participants were not required to keep a dietary and physical activity record. Upon completion of the laboratory visit portion of the study, all participants were compensated with $60. East Asians were compensated with an additional $40 for the 3-day food and activity monitoring.

4.4. Biochemical Analyses

Blood for glucose was collected in sodium fluoride tubes, centrifuged, and measured within one hour using an YSI Lactate/Glucose Analyzer at the HPL. Blood for insulin was collected in EDTA tube, immediately placed on ice, and centrifuged within 30 min for separation of plasma from the red blood cells. Plasma glucose concentrations were measured within 1 hr using a YSI Lactate/Glucose Analyzer.

Insulin was measured by standard radioimmunoassays (RIA) (Diagnostic Systems Laboratories, Inc., Webster, Texas: DSL-1600 kit). The assay of insulin was performed by the principal investigator (Su-Jong Kim) in the Department of Military Emergency Medicine, USUHS. The plasma samples were kept frozen at -80 C and assayed in batches to reduce variability. All samples were assayed in duplicates and both intra-assay and inter-assay coefficient of variations (CV) were less than 10%.

Blood for cortisol was also collected, and the plasma cortisol (total cortisol) level was measured by using the ELASA method (Diagnostic Systems Laboratories, Inc. Webster, Texas: DSL-10-2000 kit). Cortisol was measured because cortisol may be related to both obesity and insulin resistance (Bjorntorp, 2001; Bjorntorp & Rosmond, 2000). All frozen plasma samples for cortisol were sent out to the Department of Laboratory Medicine at the National Institutes of Health, Bethesda, to be analyzed (Supervisor: Alan T. Remaley, M.D., Ph.D.). All of the cortisol samples were sent out together and assayed at the same time to reduce the variability. The standard intra-assay CV from the mean of 12 replicates was less than 10.3% and the inter-assay CV from the mean of average duplicates for 12 separate runs was less than 12%.

4.5. Data Analyses

Power computations for the current study were conducted based on prior research studies of Asian populations and the preliminary data from the HPL. The proposed investigation has 2 (ethnicity) x 2 (weight) between subjects design for

Aims 1 and 2. Studies examining anthropometric and metabolic measures between East Asians and Caucasians in different BMI category groups are limited. Most studies examined only normal weight individuals or did not distinguish between different weight groups. Therefore, based on prior research studies of normal weight Asians and CA, effect sizes were estimated using independent *t*-tests. Additionally, using the data from the HPL, the differences between normal weight and overweight groups were estimated. These effect sizes were used to calculate the sample sizes necessary for the 2 x 2 between subjects design. The number of participants needed for the current study was determined using the nQuery Adivsory power calculation software package (nQuery Advisor 4.0, 1995-2000). Detailed power computations and the proposed data analyses for each aim are provided below. The statistical significance level was set at < .05, and the computer package SPSS was used for statistical analyses.

4.5.1. Data Analytic Strategy and Power Computations for Each Aim

Specific Aim 1: Determine the relationship of anthropometric measures (WHR, WC, and body fat) and metabolic measures (glucose, insulin, and insulin resistance) as a function of weight status in East Asians in comparison to Caucasians.

Power Computation: Based on prior research comparing Asians to Caucasians, the effect sizes were expected to be large (Cohen's d >1) for anthropometric measures (Z. S. Lee et al., 1999; Raji, Seely, Arky, & Simonson, 2001). Based on the preliminary data comparing the normal weight and overweight Caucasian groups, the effect sizes are estimated to be large (d>1). This effect size required 17 participants in each cell to detect between group differences with a 0.05

significance level and 80% power. The calculated effect sizes for fasting metabolic measures were vary large: d= 1.4~1.7 (Dickinson et al., 2002; Raji et al., 2001). These large effect sizes required 7 to 10 participants in each cell (N= 28~ 40) to detect between group differences with a 0.05 significance level and 80% power.

The 2 x 2 study designed was based on the fact that the previous studies did not make a distinction of the weight categories. Although studies have shown differences between Caucasian and Asian groups, no interaction of ethnicity and weight was examined because of the study design. To modify this weakness, current design employed a 2 x 2 design. For the Hypothesis 1a, b, and c, significant interaction terms were not expected. However, if any significant interaction terms exist between the two independent variables, then the 2 x 2 study design would allow them to surface.

Hypothesis 1a. East Asians would have more centrally distributed body fat (waist-circumference and waist-to-hip-ratio) and a greater percent body fat compared to BMI matched Caucasians.

Analytic Strategy: IV- Ethnicity and weight group; DVs- waist-to-hip ratio, waist circumference, and body fat percent; A 2 x 2 MANOVA was conducted to examine the difference between ethnicity and body weight groups.

Hypothesis 1b. East Asians would have higher plasma concentrations of glucose and insulin when fasting relative to BMI matched Caucasians.

Analytic Strategy: IV- Ethnicity and weight group; DVs- glucose and insulin concentrations; Two 2 x 2 ANOVA were conducted.

Hypothesis 1c. East Asians would be more insulin resistant relative to BMI matched Caucasians.

Analytic Strategy: IV- Ethnicity and weight group; DV- insulin resistance (HOMA-IR) (Matthews et al., 1985); A 2 x 2 ANOVA was conducted. HOMA-IR was used to represent insulin resistance after an overnight fast. HOMA-IR is calculated by using a formula [(fasting glucose in mmol/l) x (fasting insulin in µU/l)]/22.5 (Matthews et al., 1985).

<u>Specific Aim 2</u>: Determine the extent to which postprandial glucose and insulin concentrations differ in response to a liquid meal as a function of weight status in East Asians in comparison to Caucasians.

Power Computation: Power analyses for Aim 2 are based on the ethnic group differences using independent t-tests. Based on literature, an effect size was expected to be large (d =1.1) for postprandial metabolic measures (Dickinson et al., 2002). This effect size required 14 participants in each cell for a 2 X 2 between subjects design with a 0.05 significance level and 80% power to detect significant group differences.

Hypothesis 2a. Postprandial glucose levels would be higher in East Asians compared to BMI matched Caucasians.

Analytic Strategy: IV- Ethnicity, Weight group, and Time (5 time points over 80 minutes); DVs- levels of glucose at each time point; A 2 x 2 x 5 repeated measures ANOVA was conducted on levels of glucose. In addition, IV- Ethnicity and weight group; DVs- Peak and glucose AUC over 70 minutes (Allison, Paultre,

Maggio, Mezzitis, & Pi-Sunyer, 1995; Tai, 1994); A 2 x 2 MANOVA was conducted. AUC of glucose was calculated by using Tai's model (Tai, 1994). Tai's Model utilizes trapezoid rule to divide total area under the curve into small segments of triangles and rectangles. The areas of triangles and rectangles are calculated from their respective geometrical formulas. The sum of these individual areas was used to represent the total AUC in response to a meal. This method can estimate total area under a curve with precision (Allison et al., 1995; Tai, 1994). No significant between group interaction terms were expected.

Hypothesis 2b. Postprandial insulin levels would be higher in East Asians compared to BMI matched Caucasians.

Analytic Strategy: IV- Ethnicity, BMI, and Time (7 time points over 2 hours); DVs- levels of insulin at each time point; A 2 x 2 x 5 repeated measures ANOVA was conducted on levels of insulin. Additionally, IV- Ethnicity and weight group; DVs- Peak and insulin AUC over 70 minutes (Allison et al., 1995; Tai, 1994); A 2 x 2 ANOVA was conducted. Postprandial insulin resistance was estimated by insulin AUC. No between group interaction terms were expected.

<u>Specific Aim 3</u>: Examine the extent to which acculturation to a Western lifestyle affects physical activity patterns, dietary habits, obesity, and metabolic responses in East Asians.

Power Computation: Based on prior research, the determined correlations between acculturation and diet and physical activities were in the order of 0.43 (J. Kim & Chan, 2004a). Forty participants were needed to detect a correlation of r =

0.43 with a significance level of 0.05 and 80% power. Furthermore, preliminary data analyses from the HPL study investigating physiological and endocrine correlates of obesity showed R^2=0.46 with 4 covariates (self-reported exercise and nutritional habits, abdominal obesity, and insulin resistance) in a regression model. This R^2 estimate required a sample size of 21. Thus, 34 EA participants (calculated in the Aim 1) would be sufficient to examine the proposed path model.

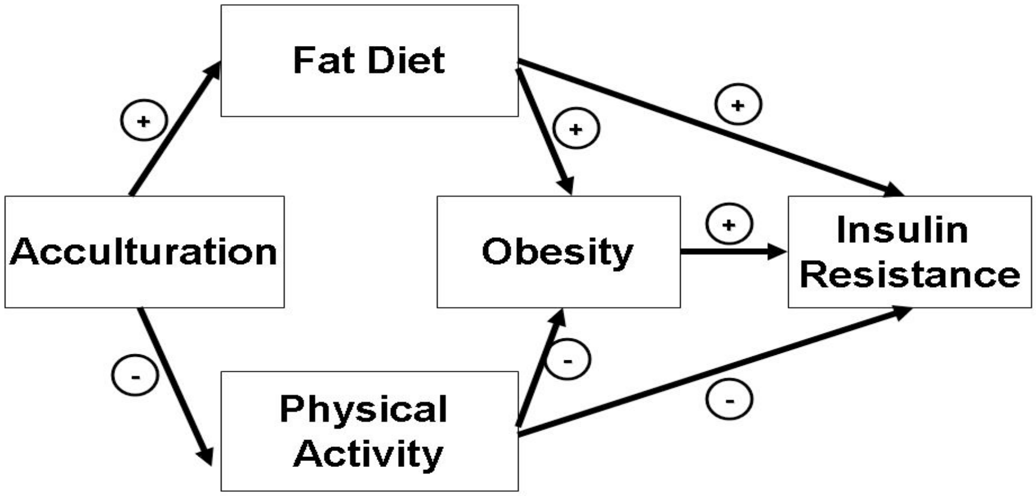
Hypothesis 3a. Increasing levels of acculturation would be positively correlated with high fat consumption and negatively associated with high physical activity.

Analytic Strategy: Variables- Acculturation, daily dietary intake, dietary fat intake, total daily energy expenditure, exercise; Correlational analyses were performed.

Hypothesis 3b. Dietary and physical activity patterns would mediate the relationship between acculturation, obesity, and consequent poor metabolic responses in East Asians.

Analytic Strategy: Exogenous variable- levels of acculturation; Intervening variables- dietary fat intake, physical activity, and BMI; DV- postprandial insulin AUC; A recursive path model testing seven paths was used to assess the direct and indirect effects of acculturation (See Figure 5). R^2 was examined first, and then standardized beta coefficients and model fit were reported.

Figure 5
A Recursive Path Model Diagram: Effects of Acculturation on the Development of Insulin Resistance



Note: A recursive path model explains the relationship among variables. The signs reflect the posited direction of the relationship between the two variables.

4.4.2. Other Statistical Considerations

The years of education have been found to be associated with eating behaviors in Asians (Lv & Cason, 2004). It is conceivable that the SES is associated with the level of acculturation, and thus confounds the relationship between acculturation, eating behavior, and health outcomes. Therefore, the SES, measured in education and household income was be examined in the context of path model.

Asians have shown to be prone to develop insulin secretory abnormality (β-cell dysfunctions) (Zimmet, 1999), and such differences are postulated to underlie the differing relationship between obesity and its metabolic consequences in East Asians. Thus, β-cell function (sensitivity to glucose stimulation) was calculated using the early incremental insulin response and the change in the ratio of insulin to glucose levels during the first 10 minutes after the meal. These values as indices of

insulin secretion were examined to characterize pancreatic sensitivity to glucose in East Asians compared to Caucasians.

High levels of cortisol have been associated with central obesity and insulin resistance (Z. S. Lee et al., 1999; Ward et al., 2003). Chronic stress is hypothesized to relate to elevated levels of cortisol and subsequently the development of obesity and insulin resistance (Bjorntorp, 2001; Bjorntorp & Rosmond, 2000). Thus, the cortisol in the fasting state was examined for East Asians.

5. Results

The presentation of results is organized as follows: (1) Sample descriptives, (2) Results from hypothesis testing, and (3) Additional follow up analyses.

5.1. Determining the Suitability of Combining the Data Sets

Thirty seven East Asian and 18 Caucasian individuals were recruited and tested for the study. The data from an additional 22 Caucasian participants were extracted from an existing data set. In order to examine the suitability of combining the Caucasian data sets, baseline characteristics, fasting and postprandial glucose and insulin concentrations were compared between the two Caucasian groups; these data are presented next. In addition, because the existing data set monitored postprandial glucose and insulin for only 70 minutes, glucose and insulin values were compared between East Asians and Caucasians from the current study for the complete 120 minutes and up to 70 minutes. All descriptive comparisons were conducted at a significance level at < .05 without correcting for inflation of type I error rates because of the descriptive nature of the comparisons.

5.1.1. Caucasian Samples: Group Comparisons

The characteristics of Caucasian participants (n=18) from the current study were compared to a recently collected Caucasian data set (n=22). The baseline characteristics of the two Caucasian groups are shown in Table 2. The two groups were comparable in age [$t(38) = 1.11$, $p = .28$], gender [$\chi^2 (1, N = 40) = .61$, $p = .44$], and anthropometric measures [Weight: $t(38) = -1.32$, $p = .20$; Height: $t(38) = -.90$, p

= .38, 7; BMI: $t(38) = -1.14$, $p = .26$; & BMI category: χ^2 (1, $N = 40$) = .97, $p = .32$]. Furthermore, the baseline fasting glucose and insulin concentrations did not differ between the two groups [$t(38) = -.42$, $p = .68$ & $t(38) = -1.29$, $p = .21$, respectively].

Table 2
Comparisons of Baseline Anthropometric and Fasting Glucose and Insulin Measures of the Two Caucasian Groups in the Study

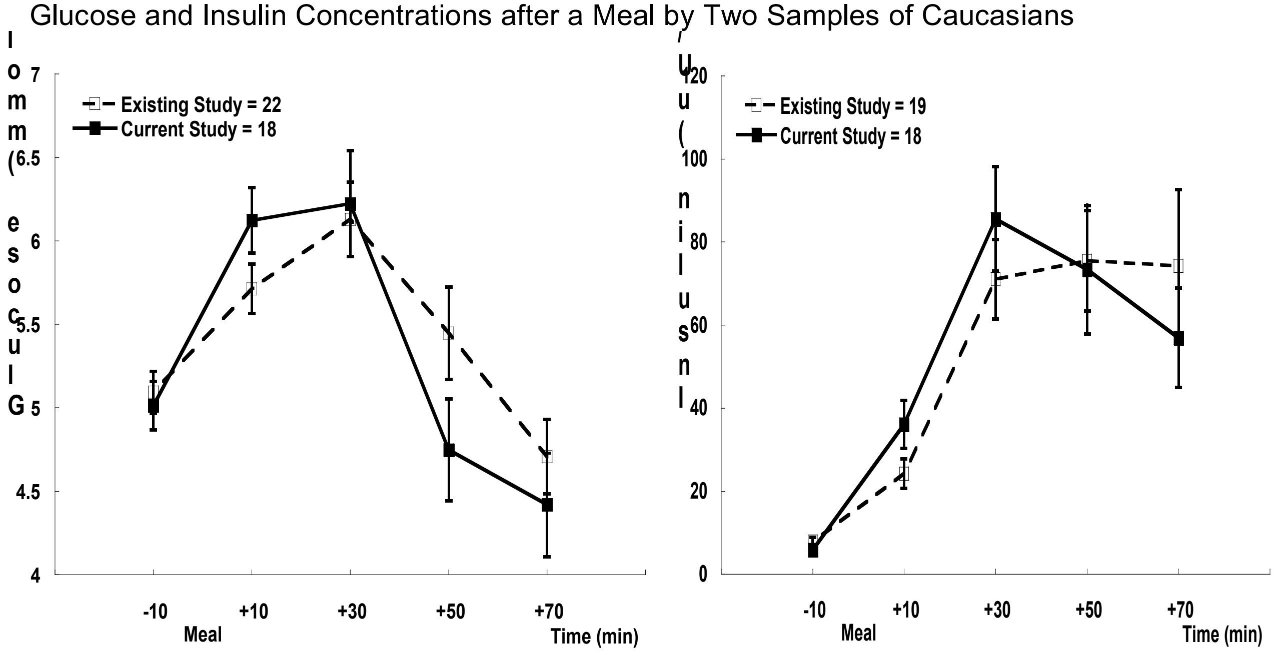
	Current Study n=18	Existing Study n=22
	Mean (SD)	
Age (yrs)	29.0 (5.1)	27.2 (5.0)
Weight (kg)	68.8 (15.2)	76.3 (19.5)
Height (cm)	168.4 (13.9)	172.0 (11.9)
BMI (kg/m^2)	24.1 (3.0)	25.3 (3.8)
Fasting Glucose (mmol/l)	5.1 (.62)	5.1 (.59)
Fasting Insulin (_U/ml)	5.87 (3.5)	7.52 (4.4)
	Count (%)	
BMI group (Normal-Wt/Over-Wt)	11 (61.1%) / 7 (38.9%)	10 (45.5%) / 12 (54.5%)
Gender (women/men)	12 (66.7%) / 6 (33.3%)	12 (54.5%) / 10 (45.5%)

Note: None of the independent t-test comparisons revealed significant difference between the two Caucasian groups.

In addition to the baseline measurement comparisons, postprandial glucose and insulin concentrations were compared. Three cases from the existing data set had missing insulin data points (1 overweight missing 30 min time point and 2 normal weight missing 50 min time point). Thus, these 3 participants were excluded from the repeated measure ANOVA for postprandial insulin responses. Figures 6a and 6b show glucose and insulin responses plotted over a 70 minute period after ingesting a liquid meal. Repeated measure ANOVAs showed no differences between the two Caucasian groups for either of these variables [Glucose: $F(1,38)$ =

.20, *p* = .66; & Insulin: *F*(1,38) = .01, *p* = .92]. Therefore, the data for the two Caucasian groups were combined and used as one group in the data analyses.

Figure 6a & 6b
Glucose and Insulin Concentrations after a Meal by Two Samples of Caucasians

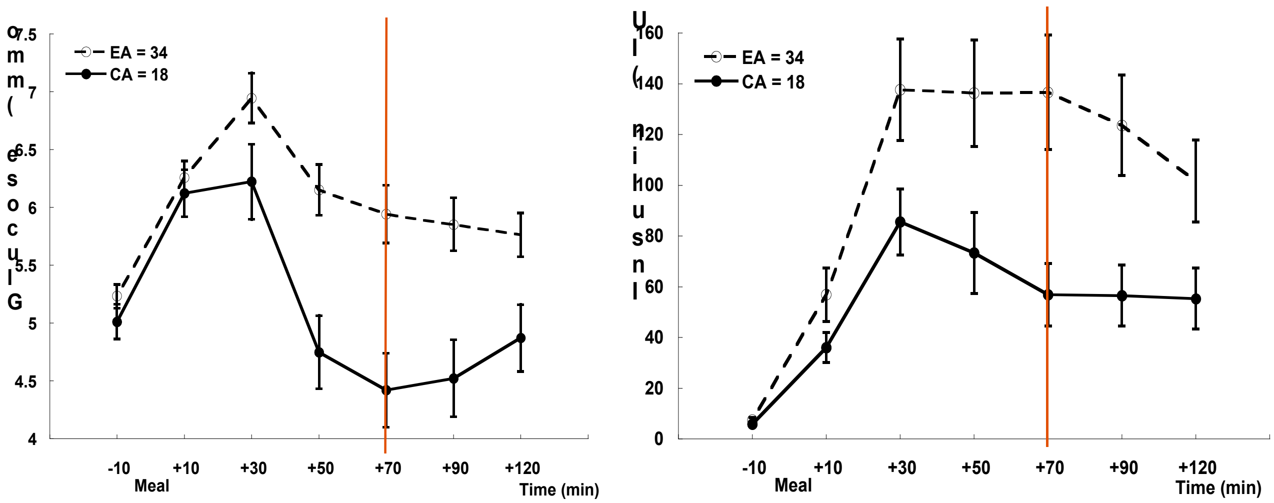


5.1.2. Postprandial Glucose and Insulin Comparisons between 70 min and 120 min of Monitoring Period

Although combining the two Caucasian data sets was found to be suitable (see above), it was unclear if comparing the two ethnic groups only for the first 70 minutes instead of the complete120 minutes would yield similar results. Thus, postprandial glucose and insulin for Caucasian participants from the current study (n = 18) and East Asians (n = 37) were compared over 70 and 120 minutes. Figures 7a and 7b show glucose and insulin plotted for 70 and 120 minutes after a meal. Repeated measure ANOVAs showed that the ethnic group differences were comparable between the two monitoring periods for glucose [120 min *F*(1,50) = 12.11, *p* = .001 vs. 70 min *F*(1,50) = 10.84, *p* = .002] and insulin [120 min *F*(1,50) =

7.59, p = .008 vs. 70 min $F(1,50)$ = 6.15, p = .017]. Therefore, all the analyses, including postprandial glucose and insulin, used postprandial data over the 70 minutes of monitoring and the existing Caucasian data were merged with the current data set.

Figure 7a & 7b
Glucose and Insulin Concentrations after a Meal up to 120 minutes by East Asians and Caucasians



Note: EA = East Asians, CA = Caucasians.

5.2. Descriptives

The data from 37 East Asian and 40 Caucasian individuals were used in the descriptive data analyses.

5.2.1. East Asian Participants

The East Asian group included 17 Chinese (46%), 18 Korean (49%), and 2 Japanese (5%) participants. Twenty-six participants were first generation immigrants (normal weight = 14, overweight = 12) and 11 were second generation (born in the U.S. but parents were immigrants; normal weight = 5, overweight = 6).

There were no 3rd or 4th generation participants. Detailed demographic and anthropomorphic information are presented in Table 3. Because of the small number of Japanese participants, only Chinese and Korean group differences were examined by using independent *t* and chi-square analyses. No significant differences were found between the Chinese and Korean participants for any of the demographic and anthropometric variables. However, Chinese participants were older than the Korean participants; this approached statistical significance [$t(33) = 2.01$, $p = .052$].

Table 3
Anthropometric and Demographics Data for 3 East Asian Groups (Mean (±SD) & Counts (%))

	Chinese n=17	Korean n=18	Japanese n=2
		Mean (SD)	
Age (yrs)	29.6 (7.6)	25.1 (5.8)	25.5 (3.5)
Weight (kg)	68.5 (13.8)	67.8 (13.7)	56.5 (1.6)
Height (m)	165.1 (9.0)	165.5 (8.3)	152.6 (6.5)
BMI (kg/m^2)	25.0 (3.7)	24.6 (3.7)	24.4 (2.7)
Education (yrs)	17.2 (2.6)	15.9 (3.1)	17.0 (1.4)
		Count (%)	
BMI group (NormalWt/OverWt)	9 (52.9) / 8 (47.1)	9 (50) / 9 (50)	1 (50) / 1 (50)
Gender (women/men)	12 (70.6) / 5 (29.4)	9 (50) / 9 (50)	2 (100) / 0
Education Degree			
High School	2 (11.8)	8 (44.5)	0
Associate	1 (5.9)	0	0
Bachelor	7 (41.2)	6 (33.3)	2 (100)
Master	3 (17.6)	4 (22.2)	0
Doctor	4 (23.5)	0	0
Skipped or Missing	0	0	0
Household Annual Income ($)			
<24,999	1 (5.9)	6 (33.3)	1 (50)
25,000~49,999	6 (35.3)	7 (38.9)	0
50,000~79,999	5 (29.4)	2 (11.1)	1 (50)
>80,000	3 (17.6)	2 (11.1)	0
Skipped or Missing	2 (11.8)	1 (5.6)	0

Note: Due to the small sample size of Japanese participants, one-way ANOVA and chi-squared analyses were conducted only between Chinese and Koreans.

5.2.2. East Asian and Caucasian Participants

Demographic information for participants in the study is presented in Table 4. BMI was used to create the two weight groups, thus no analyses were performed for BMI. East Asians and Caucasians were matched on gender and age; therefore these variables were examined only for the weight group differences. There were no differences in age[2] [$t(75) = -.04$, $p = .97$; normal weight = 27.6 (5.8), overweight = 27.6 (6.2)] or gender [$\chi^2(1, N = 77) = .038$, $p = .85$] between the two weight groups. In this sample, a significant proportion of Asian women were normal weight rather than overweight [$\chi^2(1, N = 37) = 12.39$, $p < .001$], but as described, the gender ratio was matched between the two ethnic groups.

[2] The participants' age ranged from 18 to 43. Three participants were 18 years old. They are defined as children under NIH guidelines.

Table 4
Anthropomorphic and Demographic Data for Ethnic Groups by Weight Groups (Mean (±SD) & Counts (%))

	East Asians			Caucasians		
	Normal Weight n=19	Overweight n=18	Total n=37	Normal Weight n=21	Overweight n=19	Total n=40
			Mean (SD)			
Age (yrs)	27.9 (6.8)	26.4 (7.1)	27.2 (6.9)	27.3 (4.8)	28.8 (5.3)	28.0 (5.1)
Weight (kg) §§§ *	57.6 (6.0)	78.0 (10.9)	67.5 (13.4)	60.7 (9.9)	86.4 (14.8)	72.9 (17.9)
Height (cm) §§§ *	161.5(7.4)	167.8 (9.3)	164.6 (8.9)	165.3(10.4)	176.1(13.0)	170.4(12.8)
BMI (kg/m^2)	22.1 (1.7)	27.6 (2.7)	24.8 (3.6)	22.1 (1.7)	27.8 (2.4)	24.8 (3.5)
Education (yrs)	17.1 (2.9)	16.1 (2.7)	16.6 (2.8)	16.4 (2.5)	16.9 (1.8)	16.7 (2.2)
			Count (%)			
Gender (women/men) §§	17 (89.5) / 2 (10.5)	6 (33) / 12 (66)	23 (62.2) / 14 (37.8)	17 (81) / 4 (19)	7 (36.8) / 12 (63.2)	24 (60) / 16 (40)
Education Degree (%)						
High School	4 (21.1)	6 (33.3)	10 (27.0)	4 (19.1)	2 (10.5)	6 (15.0)
Associate	0	1 (5.6)	1 (2.7)	3 (14.2)	0	2 (5.0)
Bachelor	7 (36.8)	8 (44.4)	15 (40.6)	6 (28.6)	10 (52.6)	17 (42.5)
Master	6 (31.6)	1 (5.6)	7 (18.9)	7 (33.3)	4 (21.1)	11 (27.5)
Doctor	2 (10.5)	2 (11.1)	4 (10.8)	1(4.8)	2 (10.5)	3 (7.5)
Skipped or Missing	0	0	0	0	1 (5.3)	1 (2.5)
Household Annual Income (%)						
<$ 24,999	3 (15.8)	5 (27.8)	8 (21.6)	7 (33.3)	3 (15.8)	10 (25.0)
5,000~49,999	6 (31.6)	7 (38.9)	13 (35.2)	10 (47.6)	9 (47.4)	19 (47.5)
50,000~79,999	4 (21.0)	4 (22.2)	8 (21.6)	1 (4.8)	2 (10.5)	3 (7.5)
>80,000	3 (15.8)	2 (11.1)	5 (13.5)	2 (9.5)	3 (15.8)	5 (12.5)
Skipped or Missing	3 (15.8)	0	3 (8.1)	1 (4.8)	2 (10.5)	3 (7.5)

Note: BMI was used to create weight groups, thus no analyses were performed for BMI. Ethnicity matched variables (age and gender) were examined only for the weight group differences.
* Ethnic group difference at $p < .05$; ** $p < .01$; and *** $p < .001$.
§ Weight group difference at $p < .05$; §§ $p < .01$; and §§§ $p < .001$.

Chi-square analyses and 2 (ethnicity) x 2 (weight group) ANOVAs were used to examine between group differences for the remaining variables. No interactions for weight [$F(1,73) = 1.13$, $p = .29$] or height [$F(1,73) = .93$, $p = .34$] were found. As expected, the overweight group was heavier [$F(1,73) = 86.37$, $p < .001$] and taller [$F(1,73) = 13.48$, p < .001] than the normal weight group. Although groups were

matched on BMI, East Asians weighed less [$F(1, 73) = 5.44$, $p < .05$] and had shorter stature [$F(1,73) = 6.60$, $p < .05$] than Caucasians. There were no interaction [$F(1,72) = 1.70$, $p = .20$] or main effects for the years of education [ethnicity: $F(1,72) = .05$, $p = .82$; & weight group: $F(1,72) = .17$, $p = .68$]. All groups were comparable in years of education completed and annual household income. A typical participant was in his/her late 20's, and college educated with an annual household income in the $25,000~49,999 range.

5.3. Hypotheses

5.3.1. Specific Aim 1. Metabolic and Anthropomorphic Comparisons by Ethnicity

Table 5 shows the means and standard deviations of the anthropometric measures, fasting glucose and insulin concentrations, and insulin resistance expressed as HOMA-IR.

5.3.1.1. Missing data and data transformation

Fasting glucose and insulin measurements were not obtained from one normal weight East Asian participant because of difficulty with the catheter insertion. Additionally, fasting insulin data for one overweight East Asian participant was 3 standard deviations above the mean of the overweight group, and thus the distribution of insulin data was skewed. A natural log transformation was performed on the fasting insulin, but normality could not be achieved. Therefore, this outlier was excluded from the data set to satisfy the normality assumption. The mean and SD values for fasting glucose include the results from 36 East Asian participants,

and the values for fasting insulin and HOMA-IR include the results from 35 East Asian participants.

5.3.1.2. Hypothesis 1a

East Asians would have more centrally distributed body fat (waist-circumference and waist-to-hip-ratio) and a greater percent body fat compared to BMI matched Caucasians. A 2 (ethnicity) x 2 (weight group) MANOVA was used to examine this hypothesis. There were no interaction [Waist: $F(1,73) = .18$, $p = .67$; WHR: $F(1,73) = .04$, $p = .85$; & % body fat: $F(1,73) = 1.03$, $p = .31$] or ethnicity main effects [Waist: $F(1,73) = .45$, $p = .51$; WHR: $F(1,73) = .04$, $p = .84$; & % body fat: $F(1,73) = 1.90$, $p = .17$] for any of the dependent variables. As expected, the overweight group had a larger waist circumference [$F(1,73)= 71.67$, $p <.001$] and waist to hip ratio [$F(1,73)= 18.45$, $p <.001$] compared to the normal weight group. Interestingly, the percent body fat did not significantly differ by weight status [$F(1,73)=.47$, $p = .50$]. The overweight and normal weight East Asians had similar percent body fat, which was comparable to that of the Caucasian overweight group. The normal weight Caucasians had approximately 3% less body fat than the three other groups although the difference was not statistically significant.

Table 5
Anthropometric and Baseline Metabolic Measures as a Function of Ethnicity and Weight Group (Mean (± SD)).

	East Asians		Caucasians	
	Normal Weight n=19	Overweight n=18	Normal Weight n=21	Overweight n=19
Waist (cm) §§§	72.2 (3.6)	86.4 (7.9)	72.7 (7.5)	88.3 (10.3)
Hip (cm) §§§	94.9 (4.2)	105.6 (6.1)	96.1 (6.3)	108.0 (6.0)
WHR §§§	.76 (.04)	.82 (.05)	.76 (.06)	.82 (.08)
% Body Fat (%)	30.6 (6.0)	30.0 (8.0)	26.8 (6.5)	29.5 (6.5)
Fasting Glucose (mmol/l) § a	4.99 (.40)	5.44 (.66)	4.98 (.66)	5.15 (.53)
Fasting Insulin (_U/ml) b	6.22 (3.33)	8.70 (7.47)	5.04 (1.24)	8.70 (5.17)
Ln Fasting Insulin §§ b	1.73 (.43)	1.88 (.41)	1.59 (.22)	2.02 (.54)
HOMA-IR b	1.41 (.85)	2.22 (2.4)	1.10 (.28)	1.97 (1.13)
Ln HOMA-IR §§§ b	.22 (.49)	.44 (.42)	.08 (.23)	.54 (.53)

Note: § Weight group difference at p < .05; §§ p < .01; and §§§ p < .001.
a n for EA group is 18 & 18, respectively.
b n for EA group is 18 & 17, respectively.

5.3.1.3. Hypothesis 1b

East Asians would have higher plasma concentrations of glucose and insulin when fasting relative to BMI matched Caucasians. A 2 x 2 ANOVA (Ethnicity x Weight Group) was used to examine the differences in fasting glucose and insulin. The natural log transformed insulin values were used for all data analyses, but the raw values for fasting insulin are presented in Table 5. The results revealed that there were no interaction terms [$F(1,72) = 1.20$, $p = .28$; $F(1,71) = 2.11$, $p = .15$] or a main effect of ethnicity [$F(1,72) = 1.37$, $p = .24$; $F(1,71) = .04$, $p = .84$] for glucose and insulin, respectively. In contrast, there were weight group differences in fasting glucose and insulin [$F(1,72) = 5.53$, $p < .05$; $F(1,72) = 7.82$, $p < .01$, respectively]. The overweight group had higher fasting glucose and insulin concentrations compared to the normal weight group.

5.3.1.4. Hypothesis 1c

East Asians would be more insulin resistant relative to BMI matched Caucasians. The original and the transformed HOMA-IR values are presented in Table 5, but only the transformed HOMA-IR values were used for data analyses. No significant interaction or ethnicity main effects were found for HOMA-IR [$F(1,71) = 1.51$, $p = .22$; $F(1,71) = .04$, $p = .84$]. There was a statistically significant difference between the two weight groups [$F(1,71) = 11.76$, $p < .001$]. The overweight group had higher HOMA-IR values compared to the normal weight group.

5.3.2. Specific Aim 2. Metabolic Change after a Meal

For Aim 2, metabolic changes after a meal were examined as a function of ethnicity and body weight. Figures 8 through 11 present means and standard errors for postprandial glucose and insulin. Repeated measure ANOVAs were used to examine glucose and insulin over time. Ethnicity and weight were between group measures and time (5 time points) was a repeated measure. In addition, a multivariate ANOVA was used for analyzing reduced forms of glucose and insulin concentrations after a meal (i.e., peak, and AUC).

5.3.2.1. Missing data and data transformation

Two normal weight and 1 overweight Asian participants' repeated glucose and insulin data were not available because of catheter problems during the laboratory visit. Distributions of glucose data at all time points were normal, and not transformed. However, insulin data were skewed and natural log transformed, and one outlier from the East Asian group was excluded from the analyses. The total

number of East Asians included in the repeated measure ANOVA was 33. The insulin data for three Caucasians were missing at different time points, and therefore excluded from the repeated measure ANOVA. The values for insulin peak and AUC were not normally distributed, thus a natural log transformation was performed for both variables. The number of participants included in each group for analyses is specified with each figure.

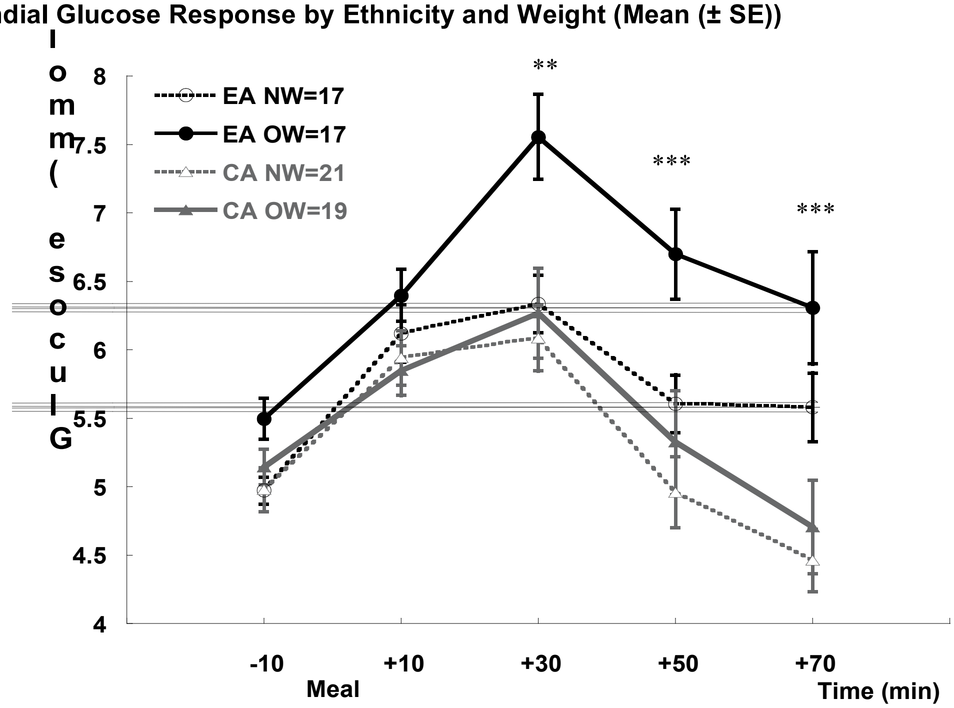
5.3.2.2. Hypothesis 2a

Postprandial glucose levels would be higher in East Asians compared to BMI matched Caucasians. Figure 8 shows postprandial glucose responses over time by groups. Mauchly's test of sphericity indicated that the assumption of sphericity had been violated for the main effects of time [χ^2 (9) =84.01, $p < .001$]. Therefore, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (ε=.631 for time effect). There was no significant three way interaction (ethnicity x weight group x time) [F(2.52, 176,59) = .59, $p = .59$] of the independent variables, and no significant weight by time [F(2.52,176,60) = 2.00, $p = .13$] or weight by ethnicity [F(1,70) = 2.76, $p = .10$] interactions. However, there was a significant ethnicity by time interaction [F(2.52,176,60) = 6.59, $p < .001$], which was subsequently examined.

Further *a priori* contrast tests revealed that the significant ethnicity by time differences were for baseline and 30 min [F(1, 70) = 6.40, $p < .05$], baseline and 50 min [F(1,70) = 9.91, $p < .01$] and baseline and 70 min [F(1,70) = 18.60, $p < .001$]. At all 3 time points, postprandial glucose concentrations were significantly higher in East Asians compared to Caucasians [30 min: F(1,70) = 8.27, $p < .01$; 50 min:

$F(1,70) = 11.95$, $p < .001$; 70 min: $F(1,70) = 20.50$, $p < .001$, respectively]. As hypothesized, there was an overall main effect of ethnicity for post meal glucose response [$F(1,70) = 16.82$, $p < .001$]. As expected, there was a main effect of weight group on postprandial glucose concentrations [$F(1,70) = 6.91$, $p < .05$], such that the overweight group had higher glucose levels than the normal weight group.

Figure 8
Postprandial Glucose Response by Ethnicity and Weight (Mean (± SE))

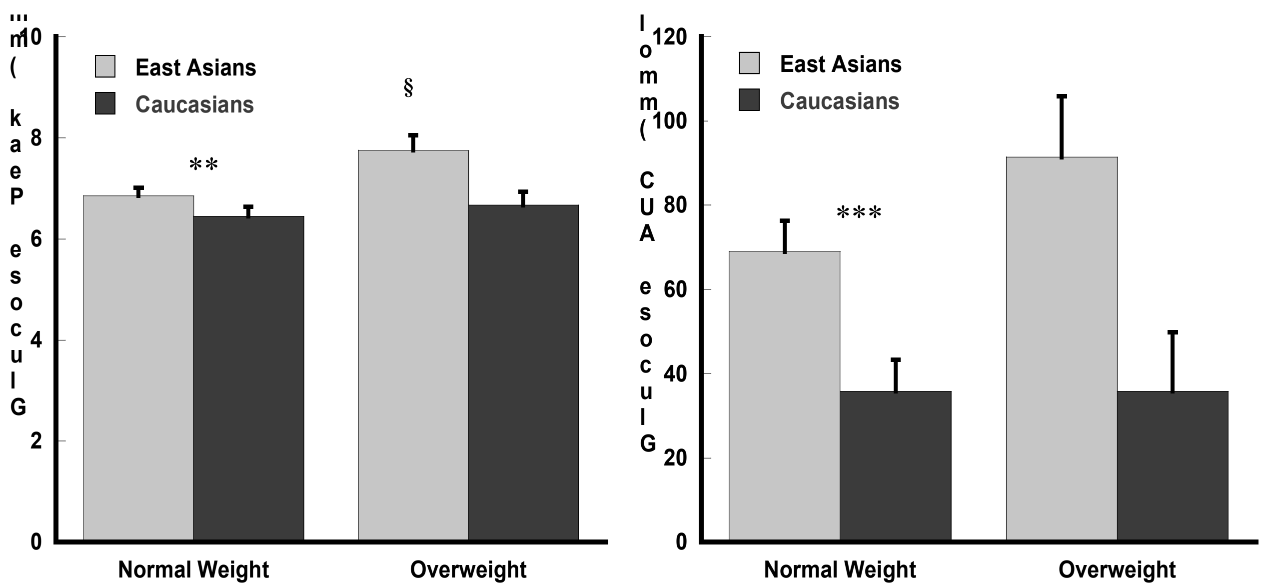


Note: EA NW = East Asian Normal Weight; EA OW = East Asian Overweight; CA NW = Caucasian Normal Weight; and CA OW = Caucasian Overweight.
* Ethnic group difference at $p < .05$; ** $p < .01$; and *** $p < .001$.

Peak postprandial glucose concentrations and AUC were examined in addition to the repeated measure analyses. Figure 9a shows the glucose peak response by groups and Figure 9b shows the total AUC for glucose over 70

minutes[3]. No ethnicity by weight group interactions were noted for the peak response or for the AUC after a meal over 70 minutes [$F(1,70) = 2.24$, $p = .14$; $F(1,70) = 1.06$, $p = .31$, respectively]. Both peak glucose and AUC were significantly higher in East Asians compared to Caucasians [$F(1,70) = 10.87$, $p < .01$; $F(1,70) = 16.41$, $p < .001$, respectively]. The glucose peak response was higher in the overweight group than in the normal weight group [$F(1,70) = 6.16$, $p < .05$], but AUC for glucose over 70 minutes did not differ by weight group [$F(1,70) = 1.04$, $p = .31$]. Interestingly, the ethnic group differences remained even after accounting for waist circumference and percent body fat [Peak: $F(1,68) = 12.7$, $p < .001$; AUC: $F(1,68) = 17.1$, $p < .001$].

Figure 9a & 9b
Glucose Peak and Area under the Curve (Mean (± SE))



Note: Normal weight East Asians = 17, Overweight East Asians = 17, Normal weight Caucasians = 21 & Overweight Caucasians = 19
* Ethnic group difference at $p < .05$; ** $p < .01$; and *** $p < .001$
§ Weight group difference at $p < .05$; §§ $p < .01$; and §§§ $p < .001$.

[3] The total time used to calculate AUC was 80 minutes: 70 minutes of postprandial monitoring period, 5 minutes between the baseline and the meal ingestion, and 5 minutes of the meal ingestion period. However, “AUC over 70 min” is used throughout to denote 70 min of the postprandial monitoring period.

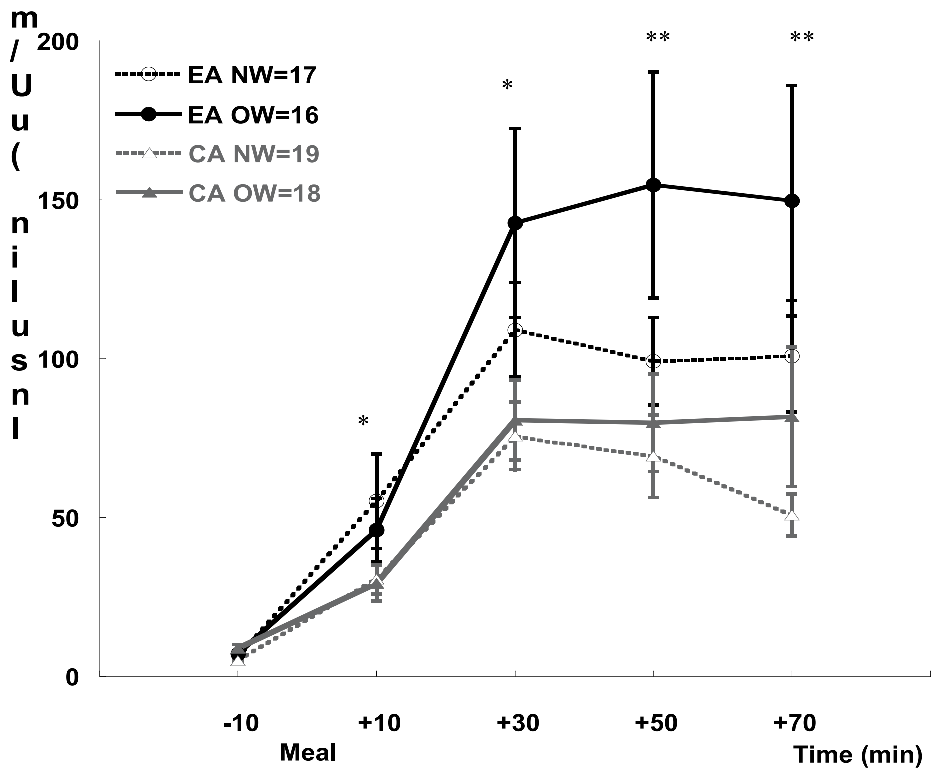
5.3.2.3. Hypothesis 2b

Postprandial insulin levels would be higher in East Asians compared to BMI matched Caucasians. Figure 10 shows the untransformed postprandial insulin concentrations over time by group. Mauchly's test of sphericity indicated that the assumption of sphericity had been violated for the main effects of time [χ^2 (9) = 42.66 $p < .001$]. Therefore the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (ε=.744 for time effect). There was no significant three-way interaction (Ethnicity x Weight x Time) [F(2.98, 196.45) = .68, p = .57], or two-way interaction terms for weight and time [F(2.98, 196.45) = 1.79, p = .15], or weight and ethnicity [F(1,66) = .01, p = .93] for postprandial insulin concentrations. However, a significant interaction between ethnicity and time was found [F(2.98, 196.45) = 4.72, $p < .01$].

Further, *a priori* contrast tests revealed that the interaction between ethnicity and time for insulin concentrations was between baseline and all time points [10 min: F(1,66) = 7.92, $p < .01$; 30 min: F(1,66) = 8.23, $p < .01$; 50 min: F(1,66) = 14,42, $p < .001$; & 70 min: F(1,66) = 13,80, $p < .001$]. East Asians had higher concentrations of insulin at all postprandial time points [10 min F(1,66) = 6.16, $p < .05$; 30 min F(1,66) = 5.03, $p < .05$; 50 min F(1,66) = 9.04, $p < .01$; & 70 min: F(1,66) = 9.10, $p < .01$]. As hypothesized, there was a significant main effect of ethnicity: East Asians produced more insulin in response to a standardized meal than Caucasians [F(1,66) = 8.02, $p < .01$].

Figure 10

Postprandial Insulin Concentrations over Time (Mean (± SE))

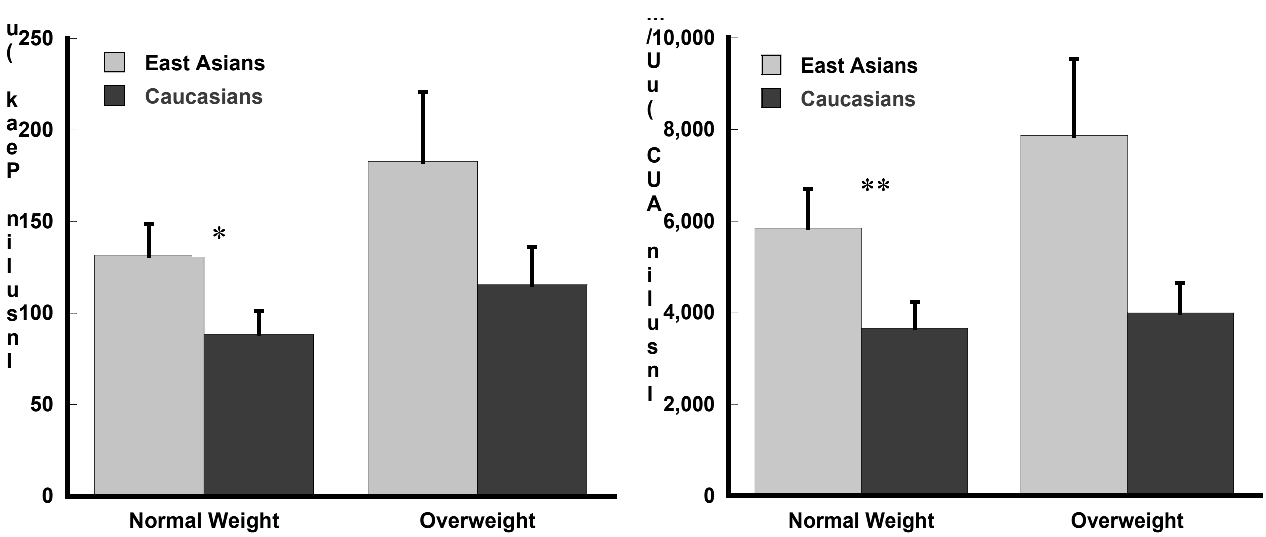


Note: EA NW = East Asian Normal Weight; EA OW = East Asian Overweight; CA NW = Caucasian Normal Weight; and CA OW = Caucasian Overweight.
* Ethnic group difference at $p < .05$; ** $p < .01$; and *** $p < .001$.

In addition to repeated measure analyses, insulin peak and AUC over time were examined. Figure 11a shows the peak insulin response by group and Figure 11b shows the total insulin AUC over 70 minutes. There were no interactions [Peak: $F(1,66) = .002$, $p = .96$; AUC: $F(1,66) = .08$, $p = .78$] or a main effect of weight [Peak: $F(1,66) = .92$, $p = .34$; AUC: $F(1,66) = .29$, $p = .60$], but the main effect of ethnicity was noted: both insulin peak and AUC were significantly higher in East Asians compared to Caucasians [$F(1,66) = 5.66$, $p < .05$ and $F(1,66) = 9.60$, $p < .01$, respectively]. The difference between ethnic groups remained even after adjusting

for waist circumference and percent body fat [Peak: $F(1,64) = 6.62$, $p < .05$; AUC: $F(1,64) = 10.65$, $p < .01$].

Figure 11a & 11b
Insulin Peak and Insulin Area under the Curve (Mean (± SE))



Note: Normal weight East Asian =17, Overweight East Asian =16, Normal weight Caucasians =19 & Overweight Caucasians =18.
* Ethnic group difference at *p* < .05; ** *p* < .01; and *** *p* < .001

5.3.3. Additional Correlational Analyses

The relationship between the variables presented in Aims 1 and 2 was examined using Pearson's product moment correlations. With regard to anthropometric and metabolic measures, BMI was significantly associated with waist circumference, percent body fat, peak glucose and insulin, insulin AUC, and HOMA-IR (Table 6). Waist circumference, a surrogate for central obesity, was positively associated with peak glucose and HOMA-IR, but not with postprandial insulin measures. Percent body fat was not associated with waist circumference but was related to postprandial insulin and HOMA-IR.

In general, the number of years of education was negatively associated with anthropometric measures and hormone responses. However, only HOMA-IR decreased significantly with increasing number of years in education. Household income was not significantly correlated with any of the variables in the analysis. Finally, age was positively associated with years of education and income, but not with any other measures.

Table 6
Correlational Analysis of the Anthropometric Measures, Hormone Responses, Education, and Household Income

		1	2	3	4	5	6	7	8	9	10
1. BMI		-									
	N										
2. Waist		.85***	-								
	N	77									
3. Body Fat %		.32**	.07	-							
	N	77	77								
4. Glucose Peak		.32**	.32**	.08	-						
	N	74	74	74							
5. Glucose AUC		0.16	.16	.17	.70***	-					
	N	74	74	74	74						
6. Ln Insulin Peak		.26**	.16	.47***	.46***	.47***	-				
	N	74	74	74	74	74					
7. Ln Insulin AUC		0.22	0.09	.48***	.45***	.50***	.98***	-			
	N	71	71	71	71	71	71				
8. Ln HOMA-IR		.62***	.49***	.40***	.39***	.26*	.60***	.56***	-		
	N	76	76	76	74	74	74	71			
9. Age		-.06	.11	-.08	.05	-.02	-.07	-.08	-.15	-	
	N	77	77	77	74	74	74	71	76		
10. Education		-.18	.01	-.02	-.07	-.06	-.03	-.05	-.25*	.61***	-
	N	76	76	76	73	73	73	70	75	76	
11. Income		.05	0.12	-.20	0.21	.19	-.03	-.02	-.03	.25*	.02
	N	74	74	74	71	71	71	70	73	74	74

Note: * Correlation is significant at $p < .05$; ** $p < .01$; and *** $p < .001$ (2-tailed).

5.3.4. Specific Aim 3. Acculturation, Lifestyle Behavior, and Metabolic Parameters among East Asians

The third aim of the study was to examine the relationship among acculturation, dietary and physical activity behaviors, and metabolic outcomes in East Asians. Tables 7, 8, and 9 show descriptive information for the psychological measures associated with acculturation, dietary and physical activity records. The results are presented by weight groups, which were defined using the NHLBI BMI cut-offs.

5.3.4.1. Missing data and data transformation

Acculturation scores were normally distributed, whereas several dietary and physical activity monitoring values were not. For the purpose of describing the data, independent *t*-tests or the two-group Mann-Whitney *U* non-parametric tests were used when the normality and equal variance assumptions were not met. For Hypothesis 3a, Pearson's r or Spearman's rho was reported as appropriate. In order to use a path analysis for Hypothesis 3b, skewed data were transformed to meet the test assumptions. Acti-heart data from four overweight participants were not available because of missing data points (n=1) or equipment malfunctions (n=3) during the monitoring period. Therefore, analyses using Acti-heart data included only 33 participants. For Hypothesis 3b, data from only 30 East Asians were available because four were missing Acti-heart data and three were missing insulin AUC data (see the Missing Data and Data Transformation section under Aim 2).

5.3.4.2. Psychological Questionnaires

The reliability of SL-ASIA was good (21 item Cronbach's alpha = .92). The mean and median scores were 2.7 and 2.67, respectively, with a minimum and maximum range of 1.67 and 4.14. According to this range, a typical participant was moderately acculturated. As a validity check, SL-ASIA for 1st generation and 2nd generation participants were compared. The mean score for the 1st generation group was 2.48 (SD = .62) and for the 2nd generation group was 3.23 (SD = .27). The difference was statistically significant [$t(35) = 3.88$, $p < .001$]. For all subscales except for the Behavior subscale, two generations significantly differed at $p < .05$. Therefore, reliability and validity of SL-ASIA for this sample was good.

Basic demographic data were compared for the overweight and normal weight East Asians. No differences in age, years of education or annual household income were noted between the groups [$t(34.72) = .64$, $p = .53$; $t(35) = 1.08$, $p = .29$; & $t(35) = -.30$, $p = .77$, respectively]. The results from the psychological questionnaires are presented in Table 7. Total scores of the SL-ASIA scale differed by group, such that the overweight group was more acculturated than the normal weight group [$t(35) = -2.21$, $p < .05$]. When the subscales (Language, Social Group, Identity, Behaviors, and Generation/Geographic) of SL-ASIA were examined, the social group [$t(35) = -2.55$, $p < .05$] and self-identity subscales [$t(35) = -2.30$, $p < .05$] differed significantly between the groups. Overweight East Asians associated with Western individuals more frequently and had a stronger Western identity than the normal weight East Asians. The remaining subscales did not differ by weight group [Language: $t(35) = -1.87$, $p = .07$; Behavior: $t(35) = -.80$, $p = .43$; &

Generation/Geographic: $t(35) = -1.50$, $p = .14$]. In addition, a trend for acculturative stress to differ by weight group was noted: the overweight group (who are more acculturated) reported less acculturative stress than the normal weight group on Acculturative Stress scale [$t(35)=1.98$, $p = .056$].

Table 7
Acculturation for Normal Weight and Overweight East Asians (Mean (± SD))

	Normal Weight	Over-Weight
Acculturation Questionnaire	n=19	n=18
Suinn-Lew Acculturation Total *	2.49 (.55)	2.93 (.66)
Language	3.03 (.90)	3.60 (.91)
Social Group *	2.26 (.66)	2.88 (.80)
Self-Identity *	2.33 (.55)	2.85 (.80)
Behaivor	2.87 (.51)	3.03 (.69)
Generation/Geographic	1.89 (.88)	2.39 (1.12)
Acculturative Stress	78.3 (22.6)	64.2 (20.3)

Note: * Group difference at $p < .05$.

5.3.4.3. Dietary Intake Reporting

Self reported dietary intake over 3 days was examined. As seen in Table 8, total calories consumed [$U(N=37) = 136.0$, $p = .30$] and the percentage of energy from each macronutrient did not differ by weight group [Protein %: $t(35) = -1.16$, $p = .25$; Fat %: $t(35) = -.23$, $p = .82$; & Carbohydrate %: $t(35) = 1.91$, $p = .07$]. Similarly, intake of none of the micronutrients differed by weight group. Dietary intake results were compared to the USDA dietary recommendations for 2,000 calories/day daily values. The USDA recommends that 10-35% of calories come from protein sources, 45-65% from carbohydrate, and 20-35% from fat (< 10% from saturated fat). Both normal weight and overweight Asians had diet compositions within the

recommended values. Table 8 also presents the intake of various vitamins, minerals and fiber. Similarly, both groups reported meeting recommended amounts of selected nutrients: cholesterol (< 300 mg), vitamin C (recommended: 90 g for men and 75 g for women), and iron (recommended: 8 mg for men and 18 mg for women) However, dietary intake of fiber (recommended: 28 g) and calcium (recommended: 1200 mg for male and1000 mg for female) were lower and sodium was higher (recommended < 2400mg) than recommended.

Table 8
Dietary Monitoring for Normal Weight and Overweight East Asians (Mean (± SD)

	Normal Weight	Over-Weight
Self-reported Dietary Intake	n=19	n=18
Daily kcal Intake (kcal)	1865 (629.5)	1925 (547.4)
Protein (g)	83 (23.6)	96 (36.5)
Protein %	18 (3.7)	20 (5.6)
Fat (g)	60 (28,7)	62 (20.2)
Fat %	29 (6.6)	29 (4.8)
Saturated Fat (g)	20 (11.8)	20 (8.5)
Saturated Fat %	9 (2.8)	9 (2.8)
Carbohydrate (g)	250 (94.8)	232 (69.8)
Carbohydrate %	53 (7.0)	49 (8.0)
Fiber (g)	18 (9.3)	13 (4.8)
Sugar (g)	74 (36.4)	72 (39.0)
Sugar to Fiber Ratio	4.5 (1.7)	6.2 (3.1)
Cholesterol (mg)	271 (118.2)	302 (162.2)
Sodium (mg)	2904 (910.8)	3304 (1306.8)
Vitamin A (I.U.)	10968 (8245.1)	6416 (4803.7)
Vitamin C (mg)	141 (134.9)	99 (63.2)
Iron (mg)	22 (12.3)	15 (5.9)
Calcium (mg)	829 (440.1)	823 (311.5)

Note: Reported data are averaged values from the 3-day dietary intake recording.

5.3.4.4. Physical Activity Reporting

The results of the physical activity records compared by weight group are presented in Table 9. Self-reported physical activity and Acti-heart physical activity

data were examined. Using the *Bouchard 3-day activity questionnaire*, weight dependent total energy expenditure values were generated. The Acti-heart data were used to generate active energy expenditure per waking hour. The active energy expenditure was generated based on heart rate and physical movement, and weight, gender, age, and resting heart rate dependent. Furthermore, the percentage of waking hours spent engaged in sedentary (set at 0 kcal/min/kg), light (< 0.031 kcal/min/kg), moderate (< 0.083 kcal/min/kg), and vigorous activities (≥ 0.083 kcal/min/kg) was obtained. Appendix 5 provides an example of Acti-heart data output and a detailed description of how the Acti-heat data were cleaned.

The *Bouchard* physical activity level differed between the two weight groups. As expected, the overweight group expended more energy during the monitoring period because of their larger body mass [$t(35) = -5.61$, $p < .001$]. In addition, active energy expenditure per hour during waking hours differed by group such that the overweight group expended more energy [$t(31) = -2.05$, $p < .05$]. If one assumes 16 waking hours, the normal weight expended on average 720 kcal/day and overweight 1,056 kcal/day. Self-reported duration of exercise per week differed by weight group [$U(N=37) = 79.5$, $p < .01$]. Normal weight East Asians [Mean Rank = 14.18, n = 19] reported spending less time exercising than overweight East Asians [Mean Rank = 24.08, n = 18]. The percentage of time spent on physical activities of different intensities did not differ by weight group [Sedentary Activity: $U(N=33) = 128.0$, $p = .87$; Light Activity: $U(N=33) = 103.0$, $p = .27$; Moderate Activity: $U(N=33) = 93.0$, $p = .15$; & Vigorous Activity: $U(N=33) = 133.0$, $p = 1.00$].

Additionally, the ratio of total daily energy intake to total energy expenditure was created to examine the energy balance. Total daily intake was from the 3-day dietary intake report and total daily energy expenditure was generated from the *Bouchard* 3-day activity questionnaire. The distribution of the ratio was skewed, and thus the comparison test was conducted with and without data transformation. Because the independent *t*-test revealed the same results, untransformed data results are reported. The ratio of energy intake to energy expenditure was significantly different between the groups [$t(35) = 2.50$, $p < .05$] such that the normal weight group had energy balance closer to 1 than the overweight group.

Table 9
Physical Activity Monitoring for Normal Weight and Overweight East Asians (Mean (± SD))

	Normal Weight	Over-Weight
Self-reported Physical Activity	n=19	n=18
Bouchard 3-Day Activity Reporting		
Energy Expenditure/Day (kcal) ***	2445 (393.1)	3220 (446.7)
Sleep (%)	39 (7.8)	35 (4.9)
Reported Exercise Min/Wk **	161 (310)	227 (135)
Actiheart Activity Monitoring	n=19	n=14
Active Energy Expenditure/hr (kcal) *	45 (22.5)	66 (35.4)
Sedentary Activity (%)	81 (13.8)	83 (6.6)
Light Activity (%)	12 (9.9)	8 (3.8)
Moderate Activity (%)	6 (4.8)	7 (3.6)
Vigorous Activity (%)	1 (1.2)	2 (2.1)
EI:EE (Energy Balance)	.78 (.23)	.60 (.17)

Note: * Group difference significant at $p < .05$; ** $p < .01$; *** $p < .001$.
EI:EE is Energy Intake to Energy Expenditure ratio. EIEE indicates the energy balance.

5.3.4.5. Hypothesis 3a

Increasing levels of acculturation would be positively correlated with high fat consumption and negatively associated with high physical activity. Correlational analyses were performed to examine this hypothesis. Table 10 shows the results of correlational analyses between acculturation and diet and physical activity. The associations between the level of acculturation and dietary factors were positive, but the relationships were not statistically significant at $p < .05$. Self-reported physical activity level and exercise data were not significantly related to acculturation [Bouchard total energy expenditure: $p = .32$; & Total exercise minutes/week: $p = .09$]. The Acti-heart results showed a positive relationship between acculturation and higher levels of active energy expenditure [$r(33) = .168$, $p = .35$]. The percent time spent engaged in different intensity activities showed that acculturation was negatively associated with sedentary activity and positively associated with light, moderate, and high intensity activity. The relationships between acculturation and physical activities were in the opposite direction of what was initially hypothesized although none of the relationships were statistically significant at $p < .05$.

Table 10
Correlational Analysis for Dietary and Physical Activity Correlates of Acculturation

	Acculturation	
	r	rho
Self-reported Dietary and Physical Activity (N= 37)		
Total Caloric Intake		.177
Fat % Intake	.063	
Total Energy Expenditure /Day	.167	
Exercise Minutes /Wk		.281
Acti-heart Physical Activity (N= 33)		
Active Energy Expenditure /Hr	.205	
Sedentary Activity %		-.190
Light Activity %		.045
Moderate Activity %		.166
Vigorous Activity %		.041

Note: * Correlation is significant at $p < .05$; ** $p < .01$; and *** $p < .001$ (2-tailed).

5.3.4.6. Hypothesis 3b

Dietary and physical activity patterns would mediate the relationship between acculturation, obesity, and consequent poor metabolic responses in East Asians. A recursive path analysis was performed to explain the relationship between acculturation, behavioral factors, obesity, and insulin resistance in East Asians. Table 11 shows the bivariate Pearson product moment correlations of the exogenous variable (acculturation) and the endogenous variables (% fat in diet, physical activity, BMI, and insulin resistance). Physical activity scores were generated by combining the percentages of time spent engaged in moderate to

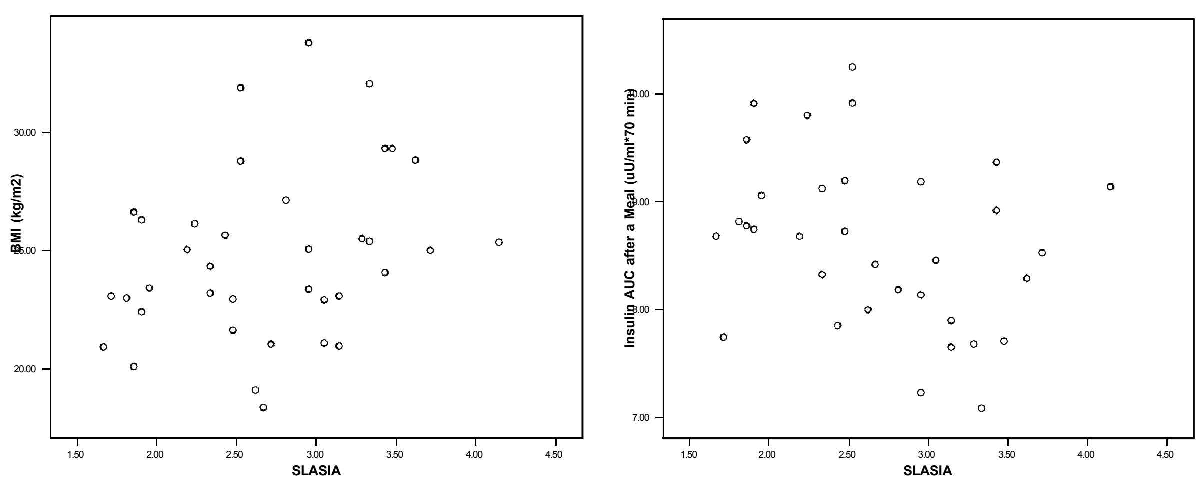
vigorous physical activity recorded by Acti-heart. Physical Activity and insulin AUC scores were natural log transformed in order to use Peason's correlations. Interestingly, the level of acculturation was negatively associated with insulin concentrations although positively associated with BMI. See scatter plots of acculturation with BMI and insulin postprandial AUC, Figure 12a and 12b.

Table 11
Correlational Analysis of the Factors in the Path Model

N = 30	1	2	3	4	5
1. Acculturation	1				
2. Physical Activity	.133	1			
3. % Fat Intake	.157	-.003	1		
4. BMI	.322*	.198	.245	1	
5. Insulin Postprandial AUC	-.289	-.377*	.161	.346*	1

Note: * Correlation is significant at $p < .05$; ** $p < .01$; and *** $p < .001$ (2-tailed).

Figure 12a & 12b
Scatter Plots between Acculturation and BMI and Postprandial Insulin AUC



Note: SLASIA = Suinn Lew Asian Self-Identity Acculturation Scale.

Table 12 shows the total, indirect, and direct effects of the path model. These effects are standardized beta coefficients (β) from multiple regression analyses. Figure 13 is a graphic representation of a path model with direct effect coefficients. R^2 for each model, direct path, and indirect paths were examined. The percentage of time engaged in moderate to vigorous activity and percent fat intake were regressed on acculturation in two separate regressions. Acculturation was not a strong predictor for high physical activity [$R^2 = .018$, $F(1,28) = .51$, $p = .48$] or a high fat diet [$R^2 = .025$, $F(1,28) = .71$, $p = .41$]. As level of acculturation increased, individuals spent more time engaged in moderate to vigorous levels of physical activity and their diet contained a higher percentage of fat although not statistically significant.

The joint effect of dietary and physical activity habits accounted for 10% of the variance in BMI [$R^2 = .10$, $F(2,27) = 1.49$, $p = .24$]. The direct effect of a high fat diet on BMI was in the positive direction and stronger [$\beta = .246$] than the effect of high physical activity on BMI [$\beta = .199$]. It should be underscored that the high physical activity was associated with increasing BMI, which is in the opposite direction from the original hypothesis. The combined effect of diet, physical activity, and acculturation accounted for 16.8% of the variance in insulin AUC [$R^2 = .168$, $F(3,26) = 1.76$, p = .18]. The indirect effects of acculturation on BMI via physical activity and high fat diet were $\beta = .026$ & $\beta = .039$, respectively.

Table 12
Standardized Direct and Indirect Effects for the Model

DV	IV	Total Effect	Indirect Effect via			Direct Effect
			Physical Activity	Dietary Fat %	BMI	
Physical Activity	Acculturation	.133				.133
Dietary Fat %	Acculturation	.157				.157
BMI	Acculturation	.065	.026	.039		
	Physical Activity	.199				.199
	Dietary Fat %	.246				.246
Insulin AUC	Acculturation	-.025	-.061	.009	.011 & .016	
	Physical Activity	-.377			.084	-.461
	Dietary Fat %	.160			.104	.056
	BMI	.423				.423

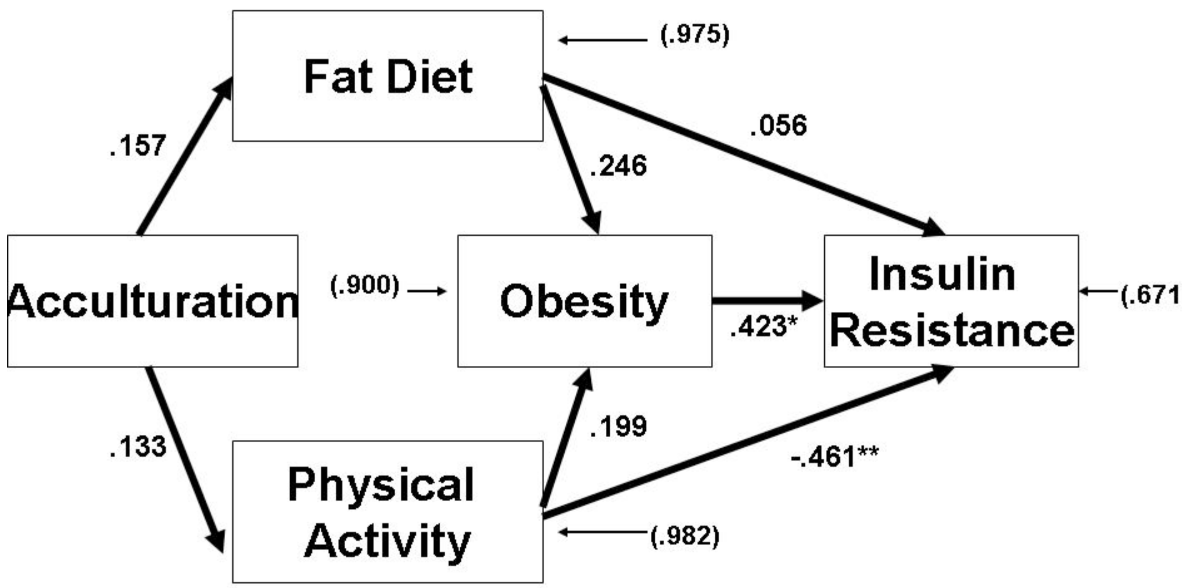
Note: The direct effect values reflect standardized β coefficients from the multiple regressions; indirect effect is generated by multiplying the direct effect coefficients between the variables; and total effect is the sum of direct and indirect effects.

The joint effect of BMI, dietary fat and physical activity accounted for 32.9% of the variance in postprandial insulin AUC [$R^2 = .329$, $F(3,26) = 4.25$, $p < .05$]. A high level of physical activity was a strong predictor of reduced postprandial insulin production [β = -.461], whereas the indirect effect of physical activity via BMI was much weaker [β = .084]. The direct effect of a diet high in fat on the postprandial insulin AUC, unlike physical activity, was not strong [β = .056]. The indirect effect of diet high in fat via BMI, however, was stronger than the direct effect of fat diet [β = .104].

The overall amount of variance in postprandial insulin AUC explained by all predictors combined (acculturation, diet, physical activity, and BMI) was 48.6% [$R^2 = .486$, $F(4,25) = 5.91$, $p < .01$]. These data suggest that the impact of dietary fat intake on insulin resistance was via an increased body weight more so than a direct

effect, whereas physical activity directly reduced insulin production. However, it should also be noted that, unlike the original hypothesis, increasing level of acculturation was positively associated with high physical activity and increasing postprandial AUC. High physical activity was associated with increasing BMI although these relationships were not significant at *p* < .05.

Figure 13
A Recursive Path Diagram Depicting the Influence of Acculturation on Obesity and Consequent Insulin Responses via Diet and Physical Activity



Note: Path diagram depicts the proposed model of the relationship between acculturation and obesity and insulin resistance via behavior factors (diet and physical activity) with standardized β coefficients. The coefficients are from the multiple regressions. The values in the parenthesis represent the variance of the errors, $1-R^2$.
* β coefficient is significant at *p* < .05; ** *p* < .01; and *** *p* < .001 (2-tailed).

A model fit was examined. Table 13 shows implied correlations with absolute differences between the implied and observed bivariate correlations in Table 12. The differences between the implied and observed correlations were averaged. The average of absolute differences for the model was .067; however, the average encompassed a wide range of residuals between .0 and .264. In particular, the

relationships between the exogenous variable and BMI and insulin AUC have shown high discrepancies between the observed and calculated. This suggests that some parts of the model may not explain the observed data adequately.

Table 13
Implied Correlations (Below the Diagonals) and Absolute Values of Residuals (Above the Diagonals) for the Model

Variable	1	2	3	4	5
1. Acculturation	-	.000	.000	.257	.264
2. Physical Activity	.133	-	-	.001	.000
3. % Fat Intake	.157	-	-	.001	.001
4. BMI	.065	.199	.246	-	.077
5. Insulin Postprandial AUC	-.025	-.377	.160	.423	-

Note: Correlations below the diagonals are the implied correlations, in this case, same as the total effect from Table 12. The absolute differences between the implied correlations and the bivariate correlations (from Table 11) represent absolute values of residuals, which are provided above the diagonal. When the difference is “0”, the fit of data is considered to be perfect.

5.4. Additional Analyses

5.4.1. Education, Health Behavior, Obesity and Insulin Resistance

Socio-economic status may have an impact on obesity and insulin resistance, via dietary and physical activity behaviors. Therefore, years of education completed and household income were examined. Because 60% of the participant were foreign born and of those, 58% of the participants were recent immigrants (less than 10 years spent in the U.S,), the household income was determined to be an unstable

measure of social standing for this specific group. Thus, years of education was used as a proxy of socio-economic status and introduced into the hypothesized model as an exogenous variable. After adding years of education to the model, the overall model remained significant [$R^2 = .507$, $F(5,24)= 4.93$, $p < .01$], however the additional contribution of education to insulin resistance was not significant [$R^2 = .021$, $F(1,24)= 1.01$, $p = .33$; $\beta = -.150$, $p < .33$].

Education in place of acculturation was examined. The overall amount of variance in postprandial insulin AUC explained by all predictors combined (education, diet, physical activity, and BMI) was reduced compared to the original model with an acculturation variable [$R^2 = .341$, $F(4,25)= 3.24$, $p < .05$]. No significant associations between years of education with percent fat in diet and physical activity [$\beta = -.089$, and $\beta = .050$, respectively] were noted.

5.4.2. Stress Profile: Relationship among Diet and Physical Activity Pattern by Ethnicity

The path analysis conducted in this study showed an importance of diet and exercise in postprandial insulin AUC within the East Asian group. Thus, self-reported diet and physical activity patterns measured by Stress Profile were compared for the two ethnic groups in order to explain the interethnic difference in insulin responses. In both subscales, interethnic differences were evident. Caucasians reported engaging in exercise more frequently and intensely than East Asians [$t(75) = 3.54$, $p < .001$; CA = 57.4 (9.1), EA = 49. 8 (9.7)], and tended to follow a more healthy nutritional approach to the daily dietary habits [$t(75) = 3.53$, $p < .001$; CA = 55.9 (9.9), EA = 48.7 (7.8)]. In a regression analysis predicting the

postprandial insulin AUC (with ethnicity, BMI, diet, and exercise), diet and exercise revealed $\beta = .080$, *ns,* and $\beta = -.277$, $p < .05$, respectively.

5.4.3. β-cell Function by Ethnicity

It is possible that β-cell function differs between East Asians and Caucasians. Changes in insulin and glucose during the first 10 minutes after a meal were examined as a β-cell function surrogate measure. In response to a meal, no difference in these surrogates for β-cell function was found between the East Asians and Caucasians [t (72) = -.08, $p = .94$; EA: = 44.66 (42.9) vs. CA: = 45.65 (59.0)].

5.4.4. Fasting Morning Cortisol Concentrations and Insulin Responses in East Asians

Morning cortisol levels were examined in relation to insulin responses in East Asians. The two weight groups had different morning cortisol concentrations [$t(34) = 3.52$, $p < .01$], such that overweight East Asians had higher cortisol levels [M = 438.59, SD = 127.37] than normal weight East Asians [M = 300.74, SD = 106.67]. Although a positive correlation was found between morning cortisol and BMI [$r(36) = .44$, $p < .01$], a significant correlation between cortisol and fasting insulin concentrations [$r(36) = -.04$, $p = .83$] or insulin AUC [$r(34) = -.18$, $p = .30$] was not seen in East Asians

6. Discussion

6.1. Review of Results

The purpose of this study was to compare the metabolic responses under conditions of fasting and in response to a naturalistic meal in East Asians and Caucasians. In particular, the relationship of anthropometric measures and metabolic responses between East Asians and Caucasians were examined. With regard to East Asians, the contribution of acculturation to the metabolic responses was considered: a path model connecting acculturation, behavioral factors, body weight, and insulin production was evaluated.

6.1.1. Specific Aim 1 & 2. Anthropometric, Fasting and Postprandial Metabolic Responses by Ethnicity

In this sample, East Asians did not have a higher percent body fat, waist circumference, or waist to hip ratio compared to their Caucasian counterparts matched on gender, age, and BMI (Hypothesis 1a: not supported). The morning fasting glucose and insulin concentrations, and HOMA-IR were also comparable between the two ethnic groups (Hypothesis 1b & 1b: not supported). However, East Asians had significantly higher concentrations of circulating glucose and insulin in response to a meal (Hypothesis 2a & 2b: supported). In a previous study, hyperinsulinemia was observed in normal weight Chinese individuals after a white bread meal (Dickinson et al., 2002). Consistent with this previous study, the current study showed similar results: hyperinsulinemia after a macronutrient balanced meal in East Asians. The cause of metabolic differences is usually attributed to

interethnic variations in abdominal fat distribution. However, in the current study, even after accounting for ethnic differences in BMI, percent body fat, and waist circumference, the ethnic differences in postprandial glucose and insulin levels remained. Furthermore, because Caucasians were heavier than East Asians although they were BMI matched, the fat free mass was considered to explain the interethnic differences in postprandial glucose and insulin. The results revealed that the groups were different on fat free mass by ethnicity and weight [Ethnicity: $F(1,73) = 6.46$, $p < .05$; Weight: $F(1,73) = 49.72$, $p < .001$], but the postprandial glucose and insulin differences between East Asians and Caucasians remained even after accounting for the interethnic difference in fat free mass.

The high concentration of postprandial glucose in East Asians may be caused by either β-cell dysfunction of pancreatic cells (insulin production), insulin resistance in the body (insulin action), or both. In the current study, no ethnic group differences were found in β-cell function, as measured by changes in insulin production in response to glucose during the first 10 minutes after meal. This comparable insulin to glucose change ratio between the two ethnic groups excludes the possibility that hyperglycemia seen in East Asians is due to a lack of insulin production by the β-cells. Moreover, high circulating insulin concentrations during the entire 70 minute monitoring period further support insulin resistance in East Asians rather than β-cell dysfunction as the cause for postprandial hyperglycemia. Literature has shown that the pathogenesis of type 2 diabetes in Asian populations may involve insulin resistance rather than β-cell dysfunction (Abate & Chandalia, 2001). The comparison of postprandial glucose and insulin levels between East Asians and

Caucasians in the current study confirms ethnic differences in the pathogenesis of diabetes and the importance of insulin resistance, rather than β-cell dysfunction, in East Asians.

Interethnic differences in insulin resistance may reflect an interplay between genetic and environmental factors. Genetic factors may predispose East Asians to develop insulin resistance and may also be responsible for abdominal fat accumulation. There is an indication that even a minimal deposition of fat in the abdominal area may induce insulin resistance in Asians (Abate & Chandalia, 2001). In the current study, no ethnic differences were found in the waist circumference measurements, despite differences in postprandial insulin responses. However, detailed quantification of abdominal fat was not possible because waist circumference was the sole measure for abdominal obesity. Although used frequently, waist measurements do not differentiate visceral and subcutaneous fat or identify the specific location of fat. Quantification of fat distribution will be fruitful in elucidating the relationship between body fat and metabolic responses among different ethnic groups.

The environmental factors often associated with insulin resistance are diet and exercise. The postprandial metabolic differences between East Asians and Caucasians in the current study may be in part explained by these dietary and physical activity factors. In this study, only East Asians monitored dietary and physical activity habits for 3 days. Although ambulatory monitoring data of diet and physical activity were not available for Caucasians, self-reported dietary and exercise habits measured in the Stress Profile were available for all participants.

The Eating subscale in the Stress Profile evaluated whether a participant generally made a practice of eating well-balanced and nourishing meals and tended to skip meals. The Eating subscale also considered whether a participant monitored and limited intake of saturated fats, cholesterol, sugar, salt, and total calories. The Exercise subscale measured the level and frequency of exercise in which the participant engaged to enhance muscular tone and the cardiovascular fitness on a regular basis. In both subscales, interethnic differences were evident (See Additional Analyses section). Caucasians reported engaging in exercise more frequently and intensely and following a more healthy and nutritional diet than East Asians. As shown in the regression analysis, exercise played an important role in insulin AUC in both ethnic groups. Physical activity, regular exercise in particular, has been associated with insulin sensitivity consistently. In the current investigation, lower levels of insulin resistance in Caucasians may be explained, in part, by more frequent and intense exercise.

6.1.2. Specific Aim 3. Acculturation, Lifestyle Behavior, and Metabolic Parameters among East Asians

Although the increased level of acculturation was not significantly associated with increased dietary fat percent and lower physical activity (Hypothesis 3a: not supported), a path model revealed an interesting results. A path model was proposed to evaluate a causal relationship between acculturation and postprandial insulin AUC via mediating dietary and physical activity factors in East Asians. This finding has not been previously reported in other studies. Although the overall model was statistically significant and accounted for a significant amount of variance

in postprandial insulin, the overall fit of the model and several specific paths must be questioned (Hypothesis 3b: partially supported). In particular, the direction and relationship between acculturation and postprandial insulin AUC was opposite of expected. Moreover, the more acculturated East Asians spent more time engaged in moderate to high intensity physical activities than the less acculturated East Asians. This positive relationship between acculturation and high physical activity may be explained by the fact that exercise is a Western phenomenon. East Asian individuals with high acculturation scores may have physical activity habits similar to Caucasians, such that the results from the path analysis within East Asians may parallel the comparison made between East Asians and Caucasians in the result section.

In summary, the current study found that exercise is a significant contributor to reducing postprandial insulin production within the East Asian group as well as a contributing factor to interethnic differences between East Asians and Caucasians. In addition, exercise may be part of the Western culture to which recent immigrants are not yet accustomed.

6.2. Study limitations

6.2.1. Body Fat Measurements

Body fat was measured by using the bioelectric impedance analysis method. This method is inexpensive, relatively easy to carry out, and not invasive to the participants. However, the equation used for computing the estimated percent body

fat accounts only for gender, height and weight and does not consider differences in frame size. Furthermore, the percent body fat is indirectly estimated via body water by the impedance measures. In the current investigation, in order to increase the reliability of the body fat estimates, all participants were told to drink plenty of water the day prior to the visit. However, it was not possible to assess each participant's true hydration status, which is one of the most important factors in accurately estimating percent body fat when using a bioelectric impedance method.

Another major concern in using bioelectric impedance analysis is the assumption that the participants in the study are similar to the populations from which the equations used to calculate body fat are derived. In this study, the body fat measurements were obtained for the purpose of comparing two different ethnic groups. The body fat calculation formula was based on the NHANES survey. It is possible that the formula generated by using this survey population may not be suitable for the use in the East Asians. Comparing two different ethnic groups by using a single equation may have lowered the validity of the estimates. However, using two separate equations would make interethnic group comparison difficult. Different measures of body fat, which are not biased by existing standards or equations, such as dual X-ray absorptiometry (DXA), may be more appropriate for quantifying body fat when different ethnic groups are compared. DXA is easy to use and more accurate in measuring percent body fat. It is also the gold standard of measuring lean and fat mass; however, DXA is costly and thus was not feasible for this investigation.

6.2.2. Dietary Monitoring

Dietary intake was recorded by using a food scale and a palm type computer. The Palm Pilot m100 (Palm, Inc., Santa Clara, CA, 2000) contains an expandable database of 1,500 everyday foods and their nutritional contents. However, the data base does not contain an extensive list of ethnic food items. If the food item was not found on the list, participants were instructed to either enter a substitute food item that resembled the original dish or enter individual ingredients. The Palm Pilot m100 was selected because the Palm allows individuals to create a menu and also enter ingredients individually. However, the lack of ethnic food items in the Palm may have reduced the accuracy in dietary reporting in terms of calories and macronutrient compositions.

Another dietary reporting method considered but not pursued in the current study was food frequency questionnaires (FFQ) developed for Asian populations. However, these questionnaires are ethnic specific. In this study, three different East Asian groups were recruited, and thus a FFQ specific for each individual's ethnic background would have been required. In such case, it would be difficult to cross validate three FFQ. Alternatively, each participant could have completed all three FFQ, but scoring three questionnaires for each individual and combining the results would have been difficult and may not have been a valid method.

The Palm Pilot/food scale method has not been extensively examined in East Asian populations. Although a food scale was provided, adherence to using the scale was expected to be low because of the inconvenience of measuring every item consumed. It is likely that the participants relied on their own estimates of the

portion size of consumed food items. However, accurate estimation of portion size poses an additional challenge for individuals who follow traditional Chinese or Korean diets. A typical Chinese or Korean meal involves sharing many small dishes with others at the table. During the course of a meal, small portions of food items are taken from several shared plates. If individuals were relying on their own estimates of the portion size, it is likely that the margins of error would be high. As noted in the energy balance ratio (EIEE) (see result section), the difference of the intake and the expenditure was large, which may indicate that the accuracy of the dietary intake report was low. Different dietary intake assessment methods, other than FFQ, need to be examined extensively with East Asians to increase the accuracy of the dietary intake reporting.

6.2.3. Combining two Caucasian groups

Twenty of the Caucasian cases were selected from an existing data set. The existing study had different aims and purposes from the current investigation. The decision to combine the data was made after comparing the two Caucasian subgroups with regard to demographic and outcome variables; no differences between the two Caucasian groups were found (see Results section). Additionally, these selected cases were matched to East Asian participants recruited in the study. Although using an existing data set is not ideal, considering the resources and burden to the participants, this was considered to be reasonable.

6.2.4. Statistical Considerations

Path analysis allows the relations among the variables in an hypothesized model to be estimated, assuming that the paths depicted in the model are sufficient and accurate. Alternatively, it can be used to test if one model explains the observed data better than competing models. In the current study, only one hypothesized model was tested, thus the main emphasis of the analysis was to examine the strength of the associations among the variables. In this path analysis, a large error variance was present for the insulin AUC measure. That is, the predictors in the model could not explain a large proportion of the variance in insulin AUC. It is possible that the unexplained variance of insulin AUC could be attributed to factors or paths not specified in the model. Thus, additional factors potentially associated with the overall and partial paths should be further examined. In order to do so, a theory driven model with an appropriate sample size should be considered (Klem, 2003).

Although competing models with different predictors were not explored in this study, different paths within the proposed variables could have existed. For instance, it is possible that the direct path from acculturation to BMI, and to postprandial insulin AUC should have been specified. In the existing model, all effects of acculturation were established only through behavioral factors, including diet and physical activity. Previous studies (Hales & Barker, 2001; Tanaka et al., 2005; Yajnik, 2000) have shown that there may be a causal relationship between birth weight and diabetes, such that low birth weight may predispose adults to develop diabetes. In the current study, most of the participants were either

immigrants or 2nd generation (US born). It is probable that the fetal nutrition of the immigrants and the 2nd generation East Asians differed, and thus their birth-weight may have been different. If this is true, then a direct link between some aspects of acculturation and insulin resistance should have been specified. The unspecified relationship between birth weight and insulin resistance may explain the observed inverse correlation between increasing acculturation and insulin resistance. However, fetal nutrition or birth weight was not measured in this study, because the goal was to examine the relationship between behavioral factors and the consequent health outcomes.

6.2.5. Participants

In the current study, younger East Asian participants tended to be 2nd generation and more acculturated: acculturation was inversely associated with age and years of education. Interestingly, education was not significantly associated with household annual income in the East Asian participants. This may be explained by the fact that the 2nd generation participants were younger [$t(35) = -2.40$, $p < .05$; 2nd generation = 23.3 (4.9), Immigrants = 28.8 (7.0)] and thus had completed less number of years of education [$t(35) = -2.17$, $p < .05$; 2nd generation = 15.1 (2.4), Immigrants = 17.2 (2.8)] than the immigrant participants at the time of study participation. The intercorrelations among these variables may have made the path analysis difficult to interpret. That is, in this specific sample, demographic variables may have confounded the relationship between acculturation and the outcome variables.

Another limitation associated with participants was that a large proportion of the normal weight participants were female. Thus, the interpretation of the model may have been confounded by gender. In fact, the relationship between acculturation and BMI was stronger in men than in women [men: $r(12) = .437$, p = ns; women: $r(18) = -.008$, p = ns], whereas the relationship between acculturation and postprandial insulin AUC was stronger in women than in men [men: $r(12) = .079$, p = ns, $r(18) = -.504$, $p < .05$]. Furthermore, time spent in moderate to high physical activities was higher in men than in women [$F(1,28) = 6.42$, $p < .05$], and although not significant, the relationship between acculturation and physical activity was stronger in men ($r(12) = .187$, p = ns) than in women ($r(18) = -.078$, p = ns).

Greater energy expenditure in men in comparison to women may have been associated with the fact that men weigh more than women, and most activity monitoring devices utilize body weight in calculating the physical activity level. The current study utilized the Acti-heart, with the monitoring device placed on the chest. This device may be more accurate in measuring physical activity in comparison to devices placed on wrists (Patterson et al., 1993). However, two separate path models for each gender group could not be tested because of a small sample size. Further investigations are necessary to elucidate the role of dietary and physical activity habits as mediating factors in the relationship between acculturation and obesity and insulin resistance.

Additionally, it should be noted that the East Asian samples in this study reside in the urban area. The physical activity pattern of East Asian individuals in the urban and rural area may be different. Thus, generalizability of the physical

activity results should be limited to urban samples and cannot be extended to the East Asians who reside in rural area.

6.2.6. Measuring Acculturation

Acculturation is a complex process and measuring this construct is difficult. The SL-ASIA scale was used to measure acculturation. The SL-ASIA scale follows a multidimensional model of acculturation, which encompasses multiple domains, such as language, social groups, preferences, behaviors, self-identity, generation and geographic information. However, it should be noted that these are not the only dimensions reflecting acculturation. Furthermore, the use of this scale is generally uni-dimensional. That is, one summary score of these dimensions is created and each individual is placed on a unidirectional linear scale (individuals acculturating to the mainstream culture) (Abe-Kim, Pkazaki, and Goto, 2001). In the current study, in order to account for each aspect of acculturation, the SL-ASIA questionnaire was chosen, but summary scores of each sub-dimension were used for the analyses. The summary scores were significantly associated with generational status and duration of residency in the US. However, it should be cautioned that acculturation is more than the sum of the sub-scores of the factors listed above.

Additionally, acculturation to Western culture is characterized by a high fat diet and low physical activity. Thus, it could be interpreted that high fat intake and low physical activity equal a high level of acculturation. However, the acculturation measured in this study puts a strong emphasis on the behavioral and cognitive aspects of acculturation aside from diet and physical activity, such as communication skills and self-identity. In support, the correlations between

acculturation and dietary and physical activity habits were not strong. Furthermore, the mechanism explaining high fat diet and low physical activity as the antecedent to acculturation is difficult to explain.

6.3. Future Directions

Results from the current study suggest that without apparent obesity, East Asians had hyperglycemic and hyperinsulinemic response to a standardized meal, and this hyperinsulinemic response was positively associated with BMI and negatively associated with exercise. However, additional studies are needed to strengthen the findings in the current investigation.

Future studies should employ a larger number of participants of different generation status. In the current study, participants were either immigrants (1st generation) or 2nd generation Asians, and younger participants were born in the U.S., and thus more acculturated. Future studies should recruit participants of different generation status and stratify the groups by age and generation to minimize the variance associated with age and other demographic factors. In this study, age was positively associated with household income or years of education completed because most of the younger participants were still in school.

Studies examining dietary habits and health outcomes should pay special attention to the accurate measurement of dietary intake. Accurately measuring ethnic food intake is difficult because of different meal practices and lack of appropriate measurement methods. In order to establish a reliable relationship between dietary intake and health outcomes in Asian groups, more accurate means

of assessing dietary intake need to be developed. For example, food composites could be collected and analyzed. More extensive research studies should be conducted in the area of dietary intake assessment in East Asians.

In future research, an ambulatory study examining the effects of dietary intake on anthropometric measures and metabolic responses should be conducted. In the current study, it was shown in a laboratory setting that East Asians, regardless of BMI, percent body fat and waist circumference, exhibited hyperglycemia and hyperinsulinemia after ingesting a standardized liquid meal. This standardized meal, which was balanced in terms of macronutrients, was used to induce metabolic responses; however, the standardized meal did not necessarily represent the typical food choices for East Asians or the amounts of food individuals would self-select. It is possible that the test meal exaggerated the metabolic responses of the East Asians and made them appear more insulin resistant than they would, had they ingested a typical meal of their choice. Future studies should examine daily dietary intake in a naturalistic setting, metabolic profiles over the course of a typical day, and the interaction of these variables on short-term and long-term health outcomes. Such studies will allow the true impact of daily dietary intake on the development of insulin resistance and diabetes to be examined.

In addition, the long-term impact of exaggerated insulin responses on other health outcomes should be examined. In a previous study, a positive association was found between insulin resistance and increased rates of mortality and morbidity in dietetic patients and in healthy individuals (European Diabetes Epidemiology Group, 1999). In a different study the risk of cardiovascular death and postprandial

glucose was noted in participants with normal fasting glucose levels (de Vegt et al, 1999). Such studies have not been conducted extensively in East Asians. The relationship between postprandial insulin and glucose with cardiovascular morbidity and mortality should be examined in East Asian populations. Additionally, insulin resistance in the context of metabolic syndrome should be examined. It is generally believed that the abdominal obesity precedes insulin resistance. However, in East Asians, hyperinsulinemia was present without apparent abdominal obesity. Thus, reduced insulin sensitivity and impaired glucose tolerance may be key features in the development of metabolic syndrome. Alternatively, the precipitating factor for metabolic syndrome is different across ethnic groups. Establishing such a relationship would allow us to identify those at risk and intervene immediately to prevent development of the syndrome. A longitudinal study including multiethnic populations would allow these questions to be answered.

6.4. Implications

The findings from the current study provide important information on interethnic differences in postprandial metabolic responses, and the role of acculturation on insulin production via behavioral factors. Previous studies have examined the relationship among anthropometric characteristics, fasting metabolic measures, and responses to an oral glucose tolerance test. In this study, a more naturalistic meal, rather than a bolus of glucose, was used to stimulate insulin response. East Asians and Caucasians did not differ in fasting glucose and insulin

concentrations; however, postprandial glucose and insulin concentrations were much higher in East Asians. These differences could not be explained by any differences in anthropometric measures, whereas behavioral factors, exercise in particular, appears to serve a significant role in reducing insulin resistance.

The implications of the current investigation are three fold. First, investigators in this area should examine the impact of elevated insulin concentrations on health. Increased rates of mortality and morbidity have been reported for diabetic patients as well as in healthy individuals with high levels of postprandial insulin concentrations. A long-term investigation of individuals with elevated insulin levels in response to a meal should be conducted. Furthermore, a longitudinal study examining dietary and exercise interventions should be conducted to determine what approaches (mode, intensity, and duration) most effectively reduce prolonged postprandial hyperglycemia and hyperinsulinemia in East Asians.

Secondly, the findings from this study challenge the standard method of diagnosing patients with diabetes in the current practice of medicine. A fasting glucose test is the test currently used to diagnose diabetes in non-pregnant adults, with the 75-g oral glucose tolerance rarely being performed in practice (Standards of medical care in Diabetes, 2007). This practice compromises early detection of the disease because East Asians tend to have normal fasting glucose, but higher postprandial glucose concentrations. There is no cure for diabetes; only the symptoms can be managed and this requires extensive care. For a disease such as this, early detection and management are the best interventions. Fortunately, the American Diabetes Association recognized Asian Americans as a high-risk ethnic

group for diabetes. However, the current guideline suggests that the test should be considered or carried out more frequently if the Asian individual is overweight, defined by BMI ≥ 25 kg/m^2. In this investigation, East Asians, regardless of their anthropometric measures, exhibited high glucose concentrations after a meal. Using a BMI cutoff that does not reflect the health risks in East Asian populations will delay early detection of any abnormality, and implementation of the necessary medical treatment or lifestyle change interventions.

Lastly, findings from this study showed the importance of lifestyle modification in East Asians. Information regarding the interplay of genetic, biological, and environmental factors should be disseminated throughout East Asian communities. Community outreach programs disseminating information on diabetes, insulin resistance, genetic predisposition, and behavioral factors should be formulated. Particularly, outreach programs should emphasize the importance of exercise. In the current study, less acculturated East Asians engaged in less physical activity, yet had lower BMI and greater hyperinsulinemia in response to a meal than more acculturated East Asians. Such information has not previously been reported, but is critical for future efforts. The more recent immigrants may believe that other immediate needs, such as financial concerns, require urgent attention and that exercising on a regular basis is not important. Immigrant groups also face additional stressors specific to acculturation. Culturally sensitive exercise programs, which consider the special needs of the immigrants, should be developed and implemented for this ethnic group in the U.S.

All East Asian groups, regardless of their generational status, should be encouraged to exercise. In this study, overweight East Asians reported exercising more than normal weight East Asians. This may indicate that physical appearance rather than health is the motivating factor in exercising. Getting outwardly thin people to exercise for unseen health benefits will pose a unique challenge. Motivational factors that may encourage East Asians to exercise on a regular basis need to be examined and utilized in exercise interventions. Community outreach is a necessary first step in educating East Asians that fitness rather than thinness is the determining factor for health. Such educational programs may eventually reduce the burden of health disparities in ethnic minorities living in the U.S.

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Appendix 1

Institutional Review Board Approval Letters

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4712
www.usuhs.mil

September 19, 2006

MEMORANDUM FOR MS. SU-JONG KIM, , MEDICAL AND CLINICAL PSYCHOLOGY

SUBJECT: Final Institutional Review Board (IRB) Approval (DoD Assurance No. P60001 and FWA # 00001628) of T091CY for Human Subject Participation

Congratulations! Your no more than minimal risk research protocol T091CY entitled, "***Understanding Obesity and the Influence of Acculturation on Metabolic Responses in East Asian Populations in the United States.***" was given full review by the Uniformed Services University Institutional Review Board (IRB) on August 10, 2006 and was approved pending revisions stipulated by the IRB. These revisions have been received and reviewed and are approved. **Your approval expires on August 9, 2007.**

The purposes of this study are to: 1) determine the relationship of anthropometric measures and metabolic measures as a function of weight status in East Asians in comparison to Caucasians; 2) determine the extent to which postprandial glucose and insulin concentrations differ in response to a liquid meal as a function of weight status in East Asians in comparison to Caucasians; and 3) examine the extent to which acculturation to a Western life style affects physical activity patterns, dietary habits, obesity, and metabolic responses in East Asians.

Attached are your approved consent documents and advertisements.

Authorization to conduct this protocol will automatically terminate on August 9, 2007. If you plan to continue with data collection or analysis beyond this date, please submit a USU form 3204A/B (continuing review) to the Office of Research by **June 10, 2007**. Though we will attempt to assist you by sending you a reminder, this reporting requirement is your responsibility.

You are required to submit amendments to this protocol, changes to the informed consent document (if applicable), adverse event reports, and other information pertinent to human participation in this protocol to this office for review. No changes to this protocol may be implemented prior to IRB approval.

If you have questions regarding specific issues on your protocol, or questions of a more general nature concerning human participation in research, please contact me at 301-295-0819/9534 or mpickerel@usuhs.mil.

Margaret Pickerel
Institutional Review Board Coordinator

cc: Director, Research Administration
Chair, MPS
File

Learning to Care for Those in Harm's Way

Appendix 2

a. Telephone Screen Script for East Asians

b. Telephone Screen Script for Caucasians

c. Telephone Screen Form

Telephone Screen Script for East Asians

"Hello, my name is ________________ and I'm calling from the Uniformed Services University. I am calling you back regarding the Insulin Resistance study. Do you have about 10 to 15 minutes to answer some questions and talk about the study?"

If no: "Can I call you back?"

If yes: *go on*.

"I'd like to tell you a few things about the study first and then I'll be glad to answer any questions that you might have, OK? This study is designed to compare hormone responses to drinking a meal (EnsurePlus) in normal weight and overweight Asian and Caucasian individuals. We are interested in understanding how different ethnic groups have different blood sugar (glucose) and insulin (hormone) responses to a meal.
The study will include:

- Two visits to USU (one laboratory and one follow-up)
- Drinking a liquid meal (2 cans of Ensure-Plus)
- Blood collection
- Completing questionnaires
- Completing a 3-day dietary and activity diary

Are you still interested in participating?

If no: "Thank you for calling and your interest in this study."

IF YES: "In order to find out if you qualify to take part in this study, we must ask you some personnel questions about your physical build and some medical history questions. We will not ask for your name or address until we are sure you do qualify for the study. If you do not wish to answer any or all of the questions please let us know as we go through them."

Begin asking questions on Screening Form.

IF **DO NOT** QUALIFY:
"I am sorry, but you do not meet the requirements for this study. It means that we are looking at very specific things in specific groups. It is very important for research purposes that our groups look as similar to each other as possible.

Thank you for you interest."

IF DO QUALIFY:
"It appears based on your answers that you probably do qualify for our study. Please let me give you some more information about the study so you can decide if you are able to participate.

- The study will require 1 laboratory visit; 1 follow up visit
- During the laboratory visit,
  - you will drink 2 cans of Ensure-plus,
  - 1 indwelling catheter (small flexible needle), intravenous line (IV), will be inserted into a vein in your arm for blood drawing,
  - Fill out some questionnaires.
- The laboratory visit will take approximately 3 hours, and will begin between 7:00 and 8:00 am.
- Before your visit you will be asked not to eat after midnight the night before the laboratory visit.
- On your laboratory visit day, if your fasting glucose is >125 mg/dl, then you could be excluded from the study.
- Monitor your food intake and physical activity for 3 days
- You will be paid $100 for entire study ($60 for the laboratory visit. And $40 for 3-day diary). Compensation will be made after completing the study.

"Are you still interested?"

IF NO,

"Thank you for your call."

IF YES,

What is your name?
How can we reach you?
What is your address so we can send a copy of the Informed Consent Document?"
Do you have any questions about the study?

"We will be sending you a packet including a consent form, and the direction to the University. Would you prefer these to be e-mailed, faxed, or mailed to you?"

Telephone Screen Script for Caucasians

"Hello, my name is _________________ and I'm calling from the Uniformed Services University. I am calling you back regarding the Insulin Resistance study. Do you have about 10 to 15 minutes to answer some questions and talk about the study?"

If no: "Can I call you back?"
If yes: *go on*.

"I'd like to tell you a few things about the study first and then I'll be glad to answer any questions that you might have, OK? This study is designed to compare hormone responses to drinking a meal (EnsurePlus) in normal weight and overweight Asian and Caucasian individuals. We are interested in understanding how different ethnic groups have different blood sugar (glucose) and insulin responses to a meal.
The study will include:

- One laboratory visit to the university
- Drinking a liquid meal (2 cans of Ensure-Plus)
- Blood collection
- Completing questionnaires

Are you still interested in participating?

If no: "Thank you for calling and your interest in this study."
IF YES: "In order to find out if you qualify to take part in this study, we must ask you some personnel questions about your physical build and some medical history questions. We will not ask for your name or address until we are sure you do qualify for the study. If you do not wish to answer any or all of the questions please let us know as we go through them."

Begin asking questions on Screening Form.

IF **DO NOT** QUALIFY:
"I am sorry, but you do not meet the requirements for this study. It means that we are looking at very specific things in specific groups. It is very important for research purposes that our groups look as similar to each other as possible.

Thank you for you interest."

IF DO QUALIFY:

"It appears based on your answers that you probably do qualify for our study. Please let me give you some more information about the study so you can decide if you are able to participate.

- The study will require 1 laboratory visit
- During the laboratory visit,
  - you will drink 2 cans of Ensure-plus,
  - 1 indwelling catheter (small flexible needle), intravenous line (IV), will be inserted into a vein in your arm for blood drawing,
  - Fill out some questionnaires.
- The laboratory visit will take approximately 3 hours, and will begin between 7:00 and 8:00 am.
- Before your visit you will be asked not to eat after midnight the night before the laboratory visit.
- On your laboratory visit day, if your fasting glucose is >125 mg/dl, then you could be excluded from the study.
- You will be paid $60 for the entire study. Compensation will be made after completing the study.

"Are you still interested?"

IF NO,

"Thank you for your call."

IF YES,

What is your name?
How can we reach you?
What is your address so we can send a copy of the Informed Consent Document?"
Do you have any questions about the study?

"We will be sending you a packet including a consent form, and the direction to the University. Would you prefer these to be e-mailed, faxed, or mailed to you?"

Interviewer: ____________________________ Date:______________________

Age: (18 - 50 years) ________ Weight (lbs) __________Height (in) ___________

BMI (wt X 703 / h^2 inches): ___________
Control: ______ (< 25) Overweight/Obese: ______ ($\geq$25 to < 35)

Ethnicity: CA / EA / Other ________
If EA: Mother's side: Grand father________ Grand mother__________
Father's side: Grant father _________ Grand Mother _________

1. Are you in the military? Yes / No
2. How did you hear about our study? __________________

---

3. Does your schedule allow you to be here for your visit? Y/**N Exclusion**
4. Have you ever been told by a physician that you had:
   - **a.** Heart disease/problems: **Y**/N **Exclusion**
   - **b.** Diabetes **Y**/N **Exclusion**
   - **c.** Liver disease **Y**/N **Exclusion**
   - **d.** Pancreatic disease **Y**/N **Exclusion**
   - e. Any chronic illnesses **Y**/N **Note**
   - f. Other major medical problems **Y**/N **Note**

5. Have you been told by a psychiatrist or psychologist that you have:
   - **g.** Depression **Y**/N **Exclusion**
     - i. Have you taken an anti-depressant in the last six months? **Y**/N **Exclusion**
   - h. Eating disorder **Y**/N **Note**
     - i. What was the diagnosis? ____________________________
   - i. Any other major psychological/psychiatric problem **Y**/N **Note**

i. If Yes, what was the diagnosis:

____

ii. Have you sought treatment for any of these problems?

If Yes, when?

____

Have you been told that this condition is resolved?

____

6. Have you ever tried to hurt yourself or end your life? **Y**/ N **Exclusion**

***** Provide a number for a suicide hot-line *****

7. Are you on any regular medications including any herbal supplements? Y/N

Which ones?

Type	Dose	Treatment

8. **STANDARDIZED MEAL:** Would you be willing/able to drink 16 fluid ounces of Ensure Plus? Y/**N** **Exclusion**

FOR EAST ASIANS ONLY

9. Would you be willing/able to keep and complete 3-day dietary and physical activity diary? (food diary, physical activity recording, and accelerometer) Y/**N** **Exclusion**

FOR WOMEN ONLY:

Are you pregnant or nursing? Y/N Exclusion
Are you going through menopause (or postmenopausal) Y/N Exclusion
Do you have normal menstrual cycles Y/N Note
Have you missed a period in the past 6 months? Y/N Note

How long is your menstrual cycle (i.e., 28 days)?: ______________
Date of Start of Last Period: ____________

(Dates for ind. visit: 7th day after start of period +/- 2 days)________________
If subject meets inclusion criteria, please ask for:

Name: ____

Address: ____

____

Phone: (H): ____

(W): ____

(M): ____

e-mail:____

Appendix 3

Questionnaires

a. Demographics Form
    - For Caucasian Participants
    - For East Asian Participants
b. The Suinn-Lew Asian Self-Identity Acculturation Scale (SL-ASIA scale)
c. Acculturative Stress Scale (AS)
d. 3-Day Physical Activity Record

DEMOGRAPHIC FORM FOR CAUCASIANS

ID: ___________________________________ Today's Date:___________________________

Date of Birth ___________________________ Age ___________________________

Height ___________________________ Weight ___________________________

Ethnicity:
Please check one or more.

_______ Caucasian
_______ African
_______ Hispanic or Latino
_______ American Indian
_______ Other __________________
_______ Black or African American, Non-Hispanic
_______ West Indian or Caribbean
_______ Asian
_______ Native Hawaiian or other Pacific Islander
_______ Alaskan Native

Marital Status:
Please check one.

_______ Single, Never Married
_______ Married
_______ Divorced
_______ Separated
_______ Widowed
_______ Living Together

Where were you born? ____

Education:

Highest degree earned _______________

Please circle highest grade completed:

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

Please check all that apply to you.

_______ Some high school
_______ Competed high school/GED
_______ Some College
______ Completed College
______ Partial Graduate/Professional school
______ Completed Graduate school/Professional school

Occupation: ____

Employment Status:
Please check one.

________	Retired	______	Homemaker
________	Full-time	______	Disabled
________	Part-time	______	Unemployed

Annual Household Income:
Please check next to the amount that most closely indicates your total yearly household income.

________	Below $24,999	______	$50,000-$79,999
________	$25,000-$50,000	______	Above $80,000

DEMOGRAPHIC FORM FOR ASIANS

ID: ________________________________ Today's Date:_________________________

Date of Birth ______________________ Age ______________________

Height ______________________ Weight ______________________

Ethnicity: Please check one or more.

Your Ethnic Background:

Chinese _____; Korean _____; Japanese _____
Other _____, specify ___________________________________

Your Biological Grandparents' Ethnic Background:

Your Father's Side:	Grandfather	Chinese _____; Korean _____; Japanese _____ Other _____, specify ______________
	Grandmother	Chinese _____; Korean _____; Japanese _____ Other _____, specify ______________
Your Mother's Side:	Grandfather	Chinese _____; Korean _____; Japanese _____ Other _____, specify ______________
	Grandmother	Chinese _____; Korean _____; Japanese _____ Other _____, specify ______________

Birthplace: Country ___________________________________
If **not** born in the United States,
When did you move to the U.S.? ____________ month ______________ year

Marital Status:
Please check one.

_______ Single, Never Married _______ Separated
_______ Married _______ Widowed
_______ Divorced _______ Living Together

Education:

Highest degree earned _______________

Please circle highest grade completed:

1 2 3 4 5 6 7 8 9 10 11 12   13 14 15 16   17 18 19 20 21 22

Please check all that apply to you.

________ Some high school
________ Competed high school/GED
________ Some College
______ Completed College
______ Partial Graduate/Professional school
______ Completed Graduate school/Professional school

If you were **not** born in the US and attended school somewhere else, please circle how many years of education you have completed before coming to the US:

0 1 2 3 4 5 6 7 8 9 10 11 12   13 14 15 16   17 18 19 20 21 22

Highest degree earned during that time _______________________________________

Your Current Occupation: ____

Employment Status: Please check one.

________ Retired
________ Full-time
________ Part-time
______ Homemaker
______ Disabled
______ Unemployed

Annual Household Income:
Please check next to the amount that most closely indicates your total yearly **household** income.

________ Below $24,999
________ $25,000-$50,000
______ $50,000-$79,999
______ Above $80,000

If you were **not** born in the US, please indicate your total yearly household income before you came to the US.

________ Below $24,999
________ $25,000-$50,000
______ $50,000-$79,999
______ Above $80,000

ID: ________________________________ Today's Date:_________________________

SUINN-LEW ASIAN SELF-IDENTITY ACCULTURATION SCALE (SL-ASIA)

INSTRUCTIONS: The questions which follow are for the purpose of collecting information about your historical background as well as more recent behaviors which may be related to your cultural identity. Choose the one answer which best describes you.

1. What language can you speak?
    1. Asian only (for example, Chinese, Japanese, Korean, etc.)
    2. Mostly Asian, some English
    3. Asian and English about equally well (bilingual)
    4. Mostly English, some Asian
    5. Only English

2. What language do you prefer?
    1. Asian only (for example, Chinese, Japanese, Korean, etc.)
    2. Mostly Asian, some English
    3. Asian and English about equally well (bilingual)
    4. Mostly English, some Asian
    5. Only English

3. How do you identify yourself?
    1. Oriental
    2. Asian
    3. Asian-American
    4. Chinese-American, Japanese-American, Korean-American, etc.
    5. American

4. Which identification does (did) your mother use?
    1. Oriental
    2. Asian
    3. Asian-American
    4. Chinese-American, Japanese-American, Korean-American, etc.
    5. American

5. Which identification does (did) your father use?
    1. Oriental
    2. Asian
    3. Asian-American
    4. Chinese-American, Japanese-American, Korean-American, etc.
    5. American

6. What was the ethnic origin of the friends and peers you had, as a child up to age 6?
   1. Almost exclusively Asians, Asian-Americans, Orientals
   2. Mostly Asians, Asian-Americans, Orientals
   3. About equally Asian groups and Anglo groups
   4. Mostly Anglos, Blacks, Hispanics, or other non-Asian ethnic groups
   5. Almost exclusively Anglos, Blacks, Hispanics, or other non-Asian ethnic groups

7. What was the ethnic origin of the friends and peers you had, as a child from 6 to 18?
   1. Almost exclusively Asians, Asian-Americans, Orientals
   2. Mostly Asians, Asian-Americans, Orientals
   3. About equally Asian groups and Anglo groups
   4. Mostly Anglos, Blacks, Hispanics, or other non-Asian ethnic groups
   5. Almost exclusively Anglos, Blacks, Hispanics, or other non-Asian ethnic groups

8. Whom do you now associate with in the community?
   1. Almost exclusively Asians, Asian-Americans, Orientals
   2. Mostly Asians, Asian-Americans, Orientals
   3. About equally Asian groups and Anglo groups
   4. Mostly Anglos, Blacks, Hispanics, or other non-Asian ethnic groups
   5. Almost exclusively Anglos, Blacks, Hispanics, or other non-Asian ethnic groups

9. If you could pick, whom would you prefer to associate with in the community?
   1. Almost exclusively Asians, Asian-Americans, Orientals
   2. Mostly Asians, Asian-Americans, Orientals
   3. About equally Asian groups and Anglo groups
   4. Mostly Anglos, Blacks, Hispanics, or other non-Asian ethnic groups
   5. Almost exclusively Anglos, Blacks, Hispanics, or other non-Asian ethnic groups

10. What is your music preference?
   1. Only Asian music (for example, Chinese, Japanese, Korean, etc.)
   2. Mostly Asian
   3. Equally Asian and English
   4. Mostly English
   5. English only

11. What is your movie preference?
    1. Asian-language movies only
    2. Asian-language movies mostly
    3. Equally Asian/English English-language movies
    4. Mostly English-language movies only
    5. English-language movies only

12. What generation are you?
    1. 1st Generation = I was born in Asia or country other than U.S.
    2. 2nd Generation = I was born in U.S., either parent was born in Asia or country other than U.S.
    3. 3rd Generation = I was born in U.S., both parents were born in U.S, and all grandparents born in Asia or country other than U.S.
    4. 4th Generation = I was born in U.S., both parents were born in U.S, and at least one grandparent born in Asia or country other than U.S. and one grandparent born in U.S.
    5. 5th Generation = I was born in U.S., both parents were born in U.S., and all grandparents also born in U.S.
    6. Don't know what generation best fits since I lack some information.

13. Where were you raised?
    1. In Asia only
    2. Mostly in Asia, some in U.S.
    3. Equally in Asia and U.S.
    4. Mostly in U.S., some in Asia
    5. In U.S. only

14. What contact have you had with Asia?
    1. Raised one year or more in Asia
    2. Lived for less than one year in Asia
    3. Occasional visits to Asia
    4. Occasional communications (letters, phone calls, etc.) with people in Asia
    5. No exposure or communications with people in Asia

15. What is your food preference at home?
    1. Exclusively Asian food
    2. Mostly Asian food, some American
    3. About equally Asian and American
    4. Mostly American food
    5. Exclusively American food

16. What is your food preference in restaurants?
    1. Exclusively Asian food
    2. Mostly Asian food, some American
    3. About equally Asian and American
    4. Mostly American food
    5. Exclusively American food

17. Do you
    1. Read only an Asian language?
    2. Read an Asian language better than English?
    3. Read both Asian and English equally well?
    4. Read English better than an Asian language?
    5. Read only English?

18. Do you
    1. Write only an Asian language?
    2. Write an Asian language better than English?
    3. Write both Asian and English equally well?
    4. Write English better than an Asian language?
    5. Write only English?

19. If you consider yourself a member of the Asian group (Oriental, Asian, Asian-American, Chinese-American, etc., whatever term you prefer), how much pride do you have in this group?
    1. Extremely proud
    2. Moderately proud
    3. Little pride
    4. No pride but do not feel negative toward group
    5. No pride but do feel negative toward group

20. How would you rate yourself?
    1. Very Asian
    2. Mostly Asian
    3. Bicultural
    4. Mostly Westernized
    5. Very Westernized

21. Do you participate in Asian occasions, holidays, traditions, etc.?
    1. Nearly all
    2. Most of them
    3. Some of them
    4. A few of them
    5. None at all

22. Rate yourself on how much you believe in Asian values (e.g., about marriage, families, education, work):

1	2	3	4	5
(do not believe)				(strongly believe in Asian values)

23. Rate your self on how much you believe in American (Western) values:

1	2	3	4	5
(do not believe)				(strongly believe in Asian values)

24. Rate yourself on how well you fit when with other Asians of the same ethnicity:

1	2	3	4	5
(do not fit)				(fit very well)

25. Rate yourself on how well you fit when with other Americans who are non-Asian (Westerners):

1	2	3	4	5
(do not fit)				(fit very well)

26. There are many different ways in which people think of themselves. Which ONE of the following most closely describes how you view yourself?

1. I consider myself basically an Asian person (e.g., Chinese, Japanese, Korean, Vietnamese, etc.). Even though I live and work in America, I still view myself basically as an Asian person.
2. I consider myself basically as an American. Even though I have an Asian background and characteristics, I still view myself basically as an American.
3. I consider myself as an Asian-American, although deep down I always know I am an Asian.
4. I consider myself as an Asian-American, although deep down, I view myself as an American first.
5. I consider myself as an Asian-American. I have both Asian and American characteristics, and I view myself as a blend of both.

ID: _________________________________ Today's Date:__________________________

Acculturative Stress Scale

	Instruction: Choose one answer which best describes you.	**Strongly Disagree**	**Moderately Disagree**	**Not Sure**	**Moderately Agree**	**Strongly Agree**
1	Homesickness bothers me.	**1**	**2**	**3**	**4**	**5**
2	I feel uncomfortable to adjust to new foods.	**1**	**2**	**3**	**4**	**5**
3	I am treated differently in social situations.	**1**	**2**	**3**	**4**	**5**
4	Others are sarcastic toward my cultural values.	**1**	**2**	**3**	**4**	**5**
5	I feel nervous to communicate in English.	**1**	**2**	**3**	**4**	**5**
6	I feel sad living in unfamiliar surroundings.	**1**	**2**	**3**	**4**	**5**
7	I fear for my personal safety because of my different cultural background.	**1**	**2**	**3**	**4**	**5**
8	I feel intimidated to participate in social activities.	**1**	**2**	**3**	**4**	**5**
9	Others are biased toward me.	**1**	**2**	**3**	**4**	**5**
10	I feel guilty to leave my family and friends behind.	**1**	**2**	**3**	**4**	**5**
11	Many opportunities are denied to me.	**1**	**2**	**3**	**4**	**5**
12	I feel angry that my people are considered inferior here.	**1**	**2**	**3**	**4**	**5**
13	Multiple pressures are placed upon me after migration.	**1**	**2**	**3**	**4**	**5**
14	I feel that I receive unequal treatment.	**1**	**2**	**3**	**4**	**5**
15	People show hatred toward me nonverbally.	**1**	**2**	**3**	**4**	**5**
16	It hurts when people don't understand my cultural values.	**1**	**2**	**3**	**4**	**5**
17	I am denied what I deserve.	**1**	**2**	**3**	**4**	**5**
18	I frequently relocate for fear of others.	**1**	**2**	**3**	**4**	**5**
19	I feel low because of my cultural background.	**1**	**2**	**3**	**4**	**5**
20	Others don't appreciate my cultural values.	**1**	**2**	**3**	**4**	**5**
21	I miss the people and country of my origin.	**1**	**2**	**3**	**4**	**5**
22	I feel uncomfortable to adjust to new cultural values.	**1**	**2**	**3**	**4**	**5**
23	I feel that my people are discriminated against.	**1**	**2**	**3**	**4**	**5**
24	People show hatred toward me through actions.	**1**	**2**	**3**	**4**	**5**
25	I feel that my status in this society is low due to my cultural background.	**1**	**2**	**3**	**4**	**5**
26	I am treated differently because of my race.	**1**	**2**	**3**	**4**	**5**
27	I feel insecure here.	**1**	**2**	**3**	**4**	**5**
28	I don't feel a sense of belonging (community) here.	**1**	**2**	**3**	**4**	**5**
29	I am treated differently because of my color.	**1**	**2**	**3**	**4**	**5**
30	I feel sad to consider my people's problems.	**1**	**2**	**3**	**4**	**5**
31	I generally keep a low profile due to fear.	**1**	**2**	**3**	**4**	**5**
32	I feel some people don't associate with me because of my ethnicity.	**1**	**2**	**3**	**4**	**5**
33	People show hatred toward me verbally.	**1**	**2**	**3**	**4**	**5**
34	I feel guilty that I am living a different lifestyle here.	**1**	**2**	**3**	**4**	**5**
35	I feel sad leaving my relatives behind.	**1**	**2**	**3**	**4**	**5**
36	I worry about my future for not being able to decide whether to stay here or to go back.	**1**	**2**	**3**	**4**	**5**

ID: ________________________________ Today's Date:_________________________

In each box, write the activity which you have carried out during this 15 minute period. If an activity is carried out over a long period (e.g., sleeping) you can draw a continuous line in the rectangular boxes which follow until such a time when there is a change in activity.

Hour	0-15 min	15-30 min	30-45 min	45-60 min
0				
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
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19				
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21				
22				
23				

Appendix 4

Informed Consent Document

a. Informed Consent Document for East Asian Participants

b. Informed Consent Document for Caucasian Participants

Informed Consent Document
For East Asian Participants

RESEARCH STUDY TITLE: **Understanding Obesity and the Influence of Acculturation on Metabolic Responses in East Asian Populations in the United States**

PROJECT DIRECTOR: **Su-Jong Kim, M.S.**

TO PERSONS WHO AGREE TO PARTICIPATE IN THIS STUDY:

You are being invited to take part in a research study. Before you decide to be a part of this study, you need to understand the risks and benefits so that you can make an informed decision. This is known as ***informed consent***.

This consent form provides information about the research study that has been explained to you over the phone. Once you understand the study and the tests it requires, you will be asked to sign this form, if you want to take part in this study. Your decision to take part is voluntary. This means you are free to choose if you want to take part in this study. You may refuse to participate or choose to withdraw from this study at any time.

During the course of the study, if you have any questions about the study or your participation in it, you may contact one of the following:

Su-Jong Kim, M.S. at 301-295-1371
Department of Medical & Clinical Psychology, USUHS, Bethesda, MD 20814-4799

Tracy Sbrocco, Ph.D. at 301-295-9674
Department of Medical & Clinical Psychology, USUHS, Bethesda, MD 20814-4799

I. THE PURPOSE OF THIS STUDY:

The prevalence of overweight/obesity and Type 2 Diabetes has increased dramatically worldwide. Although Asians generally appear to be “thin” compared to Caucasian populations, Asians may still suffer from negative health consequences related to being overweight. In other words, Asians suffer the health risks of obesity at lower body weights. It is also believed that a Western environment plays an important role in developing obesity. We are particularly interested in the role of acculturation and associated health consequences. In order to understand different patterns of obesity, its health consequences across ethnic groups, and the effect of adopting a Western lifestyle (acculturation), the current research project is undertaken.

II. INCLUSION AND EXCLUSION CRITERIA:

If you meet the following criteria (inclusion and exclusion criteria listed below), you will be eligible to participant in this study.

Inclusion Criteria:

- Chinese, Korean, or Japanese origin
- Between 18 and 50 years old
- Body Mass Index up to 35 kg/m^2 (your weight in kilograms divided by your height in meters squared)
- Read and understand English

Exclusion Criteria:

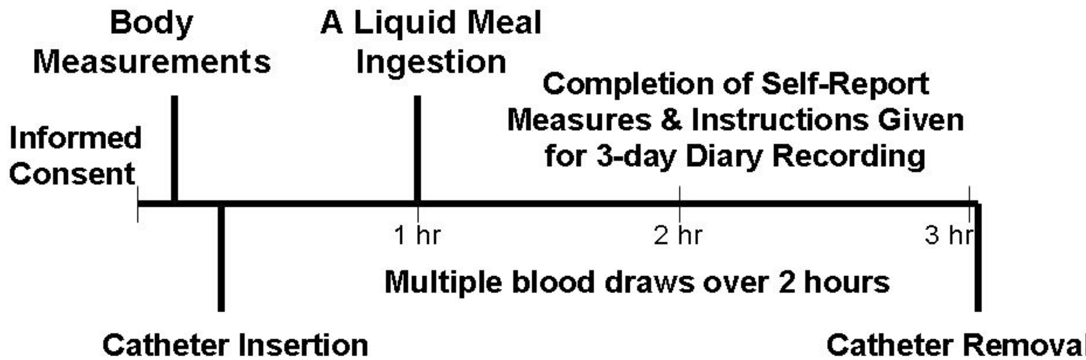
- Condition: Type 1 diabetes or Type 2 diabetes (or fasting glucose (blood sugar) >125 mg/dl during laboratory visit), liver disease, pancreatic disease, heart disease
- Use of Medications: Beta-blocker, glucose lowering agents, steroids, growth hormone, other medications that affect metabolic responses
- Suicidal thoughts; Clinically diagnosed depression or on antidepressants
- Women participants: pregnant, breast-feeding an infant

***** Women participants will be scheduled between the 5th and 9th day after the start of their period. Thus, women not having regular periods and women who may be pregnant will be eliminated from the study. Information regarding pregnancy will be asked during the phone screen process. *****

III. PROCEDURES:

Figure 1 provides a visual description of what will happen during your laboratory visit. Each of the components will be discussed further in the next sections. Your lab visit is expected to last approximately 3 hours. The lab visit will begin between 7:00 and 8:00 am, and you will be asked not to eat after midnight the night before the visit. This includes not having your breakfast on the day of your visit. We ask that you avoid drinking any alcoholic/caffeine-containing beverages and participating in any strenuous exercise for 18 hours prior to the lab visit. In addition, please drink at least 64 ounces of water over the course of the day before the visit to increase the accuracy of the body composition measure. When you come into the lab, the first thing we will do is to go over the informed consent together and answer any questions that you may have about the study.

Figure 1. Laboratory Visit Timeline



Below are brief descriptions of all study procedures, including the risks and benefits.

A. Body Measurements

Your body weight and height will be measured at the beginning of the visit. During this time, your blood pressure and heart rate will be also measured. Your body fat will be estimated at the beginning of the study by bioelectric impedance (BI). Bioelectric impedance is a method of determining body fat by measuring how a very small amount of electricity passes through the body from the hands to the feet. BI involves placing recording pads on your feet and hands and then passing a small current through your body. You will not feel the current that is passed through you, and there is no discomfort or risk with the BI measurements. We will also measure central distribution of body fat by using an inelastic measuring tape around the waist and hip.

B. Catheter Insertion & Blood Collection

During this study, you will be asked to provide blood samples. On your lab visit you will have a small plastic tube (indwelling catheter) inserted into a vein in your forearm. Blood samples will be obtained repeatedly before and after a meal (up to 8 times). Using the first blood collection, your blood glucose concentration will be determined immediately. At this point if your blood glucose is > 125 mg/dl, then you will no longer be eligible to participate in the study. We will provide a referral for you to be checked by a physician regarding a high fasting blood glucose.

Each time, approximately 10-14 ml (about 0.7-1 tablespoon) of blood will be drawn by a trained technician. The total amount of blood drawn will not exceed 120 ml (8 tablespoons). This amount is about 25% of a pint, which is 1/4 of a typical blood donation at the Red Cross. After each blood draw, the catheter line will be flushed with a 1% heparin saline solution to prevent the blood from clotting in the catheter thus interfering with blood draws. Your blood will be analyzed for glucose and hormone levels.

C. Ingestion of a Liquid Meal

You will be asked to drink 16 oz of Ensure-Plus. The meal will provide 720 kilocalories comprised of 56.4% carbohydrates, 29% fat, and 14.6% protein. Ensure is available in several flavors (vanilla, chocolate, strawberry, and butter pecan), is gluten and lactose free, kosher, and low in cholesterol. This liquid meal has been used in other studies and is known to increase your blood glucose and your body's response to a higher blood sugar. You will be given 5 minutes to drink it.

D. Interviews and Questionnaires

You will be asked to complete 8 psychological questionnaires designed to gather information relating to your eating and health habits, your life history and stresses, and overall well being. It will take approximately 70 minutes to complete these questionnaires. When filling out the questionnaires you may skip any questions you do not wish to answer. All questionnaires will be scored after completing the study; they will also be coded so that you are not personally identified on the questionnaire.

E. 3-Day Food Diary and Activity Monitoring

Upon completion of questionnaires, you will be provided with instructions on keeping an eating diary and on measuring your physical activity, including both exercise and daily life activity. To measure your food intake we will ask you to keep this diary for 3 days. You will receive a handheld personal computer (Palm m100) on loan to use for the purpose of recording your dietary intake for this study. You will also be given a portable scale to measure all foods to be consumed. Each day, you will be asked to weigh and record all foods consumed at the time of each meal, or as close to that time as possible.

During the same 3 day period, you are asked to wear an activity monitoring tool (Actiheart), and keep a daily activity diary. This activity monitoring device will be attached to your left chest via stick-on ECG electrodes. This device weighs only 10 grams and is virtually unnoticeable. You will be able to wear this activity monitor throughout the day. You have an option to take it off while you are sleeping. You MUST take it off before you shower or swim, as it is NOT water-proof. During the time you wear this device, you will self-record activities over this 3-day period. Using the forms that we provide you, you will record your activity in 15 minute intervals.

F. Follow-Up Visit

When you have completed your 3-day eating diary and physical activity monitoring, we ask that you come to USUHS for a second visit to return the

Palm m100, portable scale, Actiheart, and the activity forms. You are expected to return the computer and activity monitor after the loan period in proper working order. You will be responsible for the computer and the activity monitor in the event it is lost, stolen, or damaged.
Note: The replacement value of this computer is approximately $200.00. The replacement value of the Actiheart activity monitor is $750.00.

IV. POTENTIAL RISKS TO YOU:

- We may determine that you have a high fasting blood sugar (fasting glucose > 126 mg/dl). If so, we will provide a referral for you to be checked by a physician.
- When we insert your catheter for blood drawing, you may experience some discomfort, bruising and/or temporary pain at the site of insertion. You may also feel some discomfort and tingling or burning sensations during the injection of saline solution. In addition, there is a slight risk of infection and possibly of fainting. Sterile techniques (such as cleaning the area where the catheter will be inserted, applying a dry dressing, etc) will be used and insertion of catheters will be performed by a trained technician to reduce the risk of infection. The first blood draw will be carried out in a reclining chair to make sure you do not faint, and the saline solution will be injected slowly in order to prevent discomfort. However, if your discomfort or pain is severe, then you may decide to stop taking part in the study. We also reserve the right to remove you from the study at our discretion under such circumstances.
- There have been reports of redness and irritation on the skin associated with wearing electrodes (gel adhesives) for the physical activity monitor. To alleviate this discomfort you have an option to remove the electrodes overnight to let your skin breathe. Replacement electrodes will be provided for you. If the irritation is too severe, you can choose to discontinue the use of the Actiheart.
- You may find the questionnaires make you slightly uncomfortable, as they are somewhat private questions about stress and eating behaviors. You will NOT be forced to answer any questions that you do not want to answer.

V. POTENTIAL BENEFITS TO YOU:

The study is designed for research purposes and is not intended to be of direct benefit to you. However, at the end of the study upon your request, you will be provided with feedback on your body fat percent taken during the lab visit, and daily energy intake and expenditures taken from the 3-day monitoring period.

VI. PAYMENT:

You will be paid $100 for the completion of your participation in the study ($60 for the lab visit, and $40 for the 3-day food and activity diary). During the first hour of your lab visit, we will determine your fasting blood glucose level. If your glucose is >125 mg/dl, then you will be excluded from the study because it is one of our exclusion criteria. However, you will be compensated for your trip to the lab ($20). If you withdraw anytime after this initial glucose check and before completion of the lab visit, you will be compensated with $40 for incomplete blood draws.

All payments will be mailed to you after completing the study. To qualify for complete payment for participation in this study ($100), you must complete the lab visit and return the Palm m100 with 3 days of eating diary entries and the Actiheart with 3 days of activity recording.

Military: If you are active duty military and wish to be compensated for your participation, you must complete the form "Statement of Approval for Participation in Research" given to you by the study staff. You must inform and seek approval from your Commanders.

Federal Civilian: If you are a federal employee and wish to be compensated for your participation, you must complete the form "Statement of Approval for Participation in Research" given to you by the study staff. If you do not wish to be compensated this form does not apply, but you are strongly encouraged to inform your supervisor of your participation.

VII. RIGHT TO WITHDRAW:

You may decide to stop taking part in the study at any time. Your relations with the faculty, staff, and administration at USUHS will not change in any way if you decide to end your participation. You should let the study leader know if you decide to stop taking part. We also reserve the right to remove you and your sample from the study at our discretion if we determine that circumstances (such as failure to follow instructions, reaction to saline flush, etc) require such actions.

VIII. RECOURSE IN THE EVENT OF INJURY:

This study should not entail any physical or mental risk beyond those described above. We do not expect complications to occur, but if, for any reason, you feel that continuing this study would constitute a hardship for you, we will end your participation in the study.

In the event of a medical emergency while participating in this study or medical treatment is required as a result of your participation in this study, you may receive emergency treatment in the facility you are in or a nearby Department of Defense (military) medical facility (hospital or clinic). Treatment/care will be provided even if you are not eligible to receive such care. Care will be continued until the medical doctor treating you decides that you are out of immediate danger. If you are

not entitled to care in a military facility, you may be transferred to a private civilian hospital. The attending doctor or member of the hospital staff will go over the transfer decision with you before it happens. The military will bill your health insurance for health care you receive which is not part of the study. You will not be personally billed and you WILL NOT be expected to pay for medical care at our hospitals. If you are required to pay a deductible you may make a claim for reimbursement through the Uniformed Services University Office of General Counsel.

In case you need additional care following discharge from the military hospital or clinic, a military health care professional will decide whether your need for care is directly related to being in the study. If your need for care is related to the study, the military may offer you limited health care at its medical facilities. This additional care is not automatic.

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Office of Research at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-3303. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

IX. PRIVACY AND CONFIDENTIALITY:

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Information that you provide and other records related to this study will be accessible to those persons directly involved in conducting this study and members of the Uniformed Services University of the Health Sciences Institutional Review Board (IRB), who provide oversight for protection of human research volunteers. All questionnaires, forms, and charts will be kept in a restricted access, locked cabinet while not in use. Your blood samples, stripped off of any personal information, will be stored in a restricted access freezer over the course of the study (2 years). After verification of the database information, paper copies of all materials containing identifiers will be shredded at the end of the study. Furthermore, published data will contain no references to an identifiable individual. If you are a military member, please be advised that under Federal Law, a military member's confidentiality cannot be strictly guaranteed.

****IF YOU HAVE ANY QUESTIONS PLEASE FEEL FREE TO ASK****

By signing below, you indicate that you have read the explanation of this study on this form. The testing procedures have been reviewed and all your questions have been answered. You understand the nature of the study and

volunteer to participate in it. You attest that you meet the requirements for participation in this study. You understand that the study is designed for research purposes and not to be of direct benefit to you.

If you have any additional questions, you should contact ***Su-Jong Kim at (301) 295-1371***. If you have questions about your rights as a research participant, you should call the Director of the Human Research Protections Program in the Office of Research at USUHS (301-295-3303). This person is your representative and has no connection to the investigators conducting the studies.

I have read this consent form and I understand the procedures to be used in this study and the possible risks, inconveniences, and/or discomforts that may be involved. All of my questions have been answered. I freely and voluntarily choose to participate. I understand that I may withdraw at any time. My signature also indicates that I have received a copy of this consent form for my information.

YOU AGREE TO PARTICIPATE IN THE FOLLOWING PROCEDURES:

SCREENING EXAM	**BODY COMPOSITION EVALUATION**
BLOOD DRAWING	**QUESTIONNAIRES**
INGESTION OF A LIQUID MEAL	**3-DAY ACTIVITY MONITORING**
3-DAY FOOD DIARY	

SIGNATURES:

____________________	____________________	__________
Signature of Volunteer	Volunteer Name (Print)	Date

__________________________ ____________________________
Volunteer Address

____________________	____________________	__________
Signature of Witness	Witness Name (Print)	Date

The Principal Investigator certifies that the research study has been explained to the above individual, by the Principal Investigator or a member of the research staff, and that the individual understands the nature and purpose, the possible risks and benefits associated with taking part in this research study. Any questions that have been raised have been answered.

____________________	____________________	__________
Investigator’s Signature	Printed Name	Date

Informed Consent Document
For Caucasian Participants

RESEARCH STUDY TITLE: **Understanding Obesity and the Influence of Acculturation on Metabolic Responses in East Asian Populations in the United States**

PROJECT DIRECTOR: **Su-Jong Kim, M.S.**

TO PERSONS WHO AGREE TO PARTICIPATE IN THIS STUDY:

You are being invited to take part in a research study. Before you decide to be a part of this study, you need to understand the risks and benefits so that you can make an informed decision. This is known as ***informed consent***.

This consent form provides information about the research study that has been explained to you over the phone. Once you understand the study and the tests it requires, you will be asked to sign this form, if you want to take part in this study. Your decision to take part is voluntary. This means you are free to choose if you want to take part in this study. You may refuse to participate or choose to withdraw from this study at any time.

During the course of the study, if you have any questions about the study or your participation in it, you may contact one of the following:

Su-Jong Kim, M.S. at 301-295-1371
Department of Medical & Clinical Psychology, USUHS, Bethesda, MD 20814-4799

Tracy Sbrocco, Ph.D. at 301-295-9674
Department of Medical & Clinical Psychology, USUHS, Bethesda, MD 20814-4799

I. THE PURPOSE OF THIS STUDY:

The prevalence of overweight/obesity and Type 2 Diabetes has increased dramatically worldwide. Although Asians generally appear to be “thin” compared to Caucasian populations, Asians may still suffer from negative health consequences related to being overweight. In other words, Asians suffer the health risks of obesity at lower body weights. It is also believed that a Western environment plays an important role in developing obesity. We are particularly interested in the role of acculturation and associated health consequences. In order to understand different patterns of obesity, its health consequences across ethnic groups, and the effect of adopting a Western lifestyle (acculturation), the current research project is undertaken.

II. INCLUSION AND EXCLUSION CRITERIA:

If you meet the following criteria (inclusion and exclusion criteria listed below), you will be eligible to participant in this study.

Inclusion Criteria:

- Caucasians
- Between 18 and 50 years old
- Body Mass Index up to 35 kg/m^2 (your weight in kilograms divided by your height in meters squared)
- Read and understand English

Exclusion Criteria:

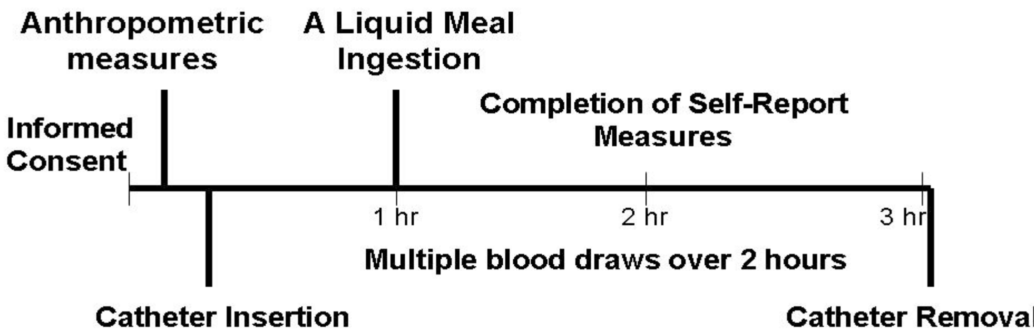
- Condition: Type 1 diabetes or Type 2 diabetes (or fasting glucose (blood sugar) >125 mg/dl during laboratory visit), liver disease, pancreatic disease, heart disease
- Use of Medications: Beta-blocker, glucose lowering agents, steroids, growth hormone, other medications that affect metabolic responses
- Suicidal thoughts; Clinically diagnosed depression or on antidepressants
- Women participants: pregnant, breast-feeding an infant

*****Women participants will be scheduled between the 5th and 9th day after the start of their period. Thus, women not having regular periods and women who may be pregnant will be eliminated from the study. Information regarding pregnancy will be asked during the phone screen process. *****

III. PROCEDURES:

Figure 1 provides a visual description of what will happen during your laboratory visit. Each of the components will be discussed further in the next sections. Your lab visit is expected to last approximately 3 hours. The lab visit will begin between 7:00 and 8:00 am, and you will be asked not to eat after midnight the night before the visit. This includes not having your breakfast on the day of your visit. We ask that you avoid drinking any alcoholic/caffeine-containing beverages and participating in any strenuous exercise for 18 hours prior to the test session. In addition, please drink at least 64 ounces of water over the course of the day before the visit to increase the accuracy of the body composition measure. When you come into the lab, the first thing we will do is to go over the informed consent together and answer any questions that you may have about the study.

Figure 1. Laboratory Visit Timeline



Below are brief descriptions of all study procedures, including the risks and benefits.

A. *Body Measurements*

Your body weight and height will be measured at the beginning of the visit. During this time, your blood pressure and heart rate will be also measured. Your body fat will be estimated at the beginning of the study by bioelectric impedance (BI). Bioelectric impedance is a method of determining body fat by measuring how a very small amount of electricity passes through the body from the hands to the feet. BI involves placing recording pads on your feet and hands and then passing a small current through your body. You will not feel the current that is passed through you, and there is no discomfort or risk with the BI measurements. We will also measure central distribution of body fat by using an inelastic measuring tape around the waist and hip.

B. *Catheter Insertion & Blood Collection*

During this study, you will be asked to provide blood samples. On your lab visit you will have a small plastic tube (indwelling catheter) inserted into a vein in your forearm. Blood samples will be obtained repeatedly before and after a meal (up to 8 times). Using the first blood collection, your blood glucose concentration will be determined immediately. At this point if your blood glucose is > 125 mg/dl, then you will no longer be eligible to participate in the study. We will provide a referral for you to be checked by a physician regarding a high fasting blood glucose.

Each time, approximately 10-14 ml (about 0.7-1 tablespoon) of blood will be drawn by a trained technician. The total amount of blood drawn will not exceed 120 ml (8 tablespoons). This amount is about 25% of a pint, which is 1/4 of a typical blood donation at the Red Cross. After each blood draw, the catheter line will be flushed with a 1% heparin saline solution to prevent the blood from clotting in the catheter thus interfering with blood draws. Your blood will be analyzed for glucose and hormone levels.

C. Ingestion of a Liquid Meal

You will be asked to drink 16 oz of Ensure-Plus. The meal will provide 720 kilocalories comprised of 56.4% carbohydrates, 29% fat, and 14.6% protein. Ensure is available in several flavors (vanilla, chocolate, strawberry, and butter pecan), is gluten and lactose free, kosher, and low in cholesterol. This liquid meal has been used in other studies and is known to increase your blood glucose and your body's response to a higher blood sugar. You will be given 5 minutes to drink it.

D. Interviews and Questionnaires

You will be asked to complete 4 psychological questionnaires designed to gather information relating to your eating and health habits, your life history and stresses, and overall well being. It will take approximately 50 minutes to complete these questionnaires. When filling out the questionnaires you may skip any questions you do not wish to answer. All questionnaires will be scored after completing the study; they will also be coded so that you are not personally identified on the questionnaire.

IV. POTENTIAL RISKS TO YOU:

- We may determine that you have a high fasting blood sugar (fasting glucose > 126 mg/dl). If so, we will provide a referral for you to be checked by a physician.
- When we insert your catheter for blood drawing, you may experience some discomfort, bruising and/or temporary pain at the site of insertion. You may also feel some discomfort and tingling or burning sensations during the injection of saline solution. In addition, there is a slight risk of infection and possibly of fainting. Sterile techniques (such as cleaning the area where the catheter will be inserted, applying a dry dressing, etc) will be used and insertion of catheters will be performed by a trained technician to reduce the risk of infection. The first blood draw will be carried out in a reclining chair to make sure you do not faint, and the saline solution will be injected slowly in order to prevent discomfort. However, if your discomfort or pain is severe, then you may decide to stop taking part in the study. We also reserve the right to remove you from the study at our discretion under such circumstances.
- You may find the questionnaires make you slightly uncomfortable, as they are somewhat private questions about stress and eating behaviors. You will NOT be forced to answer any questions that you do not want to answer.

V. POTENTIAL BENEFITS TO YOU:

The study is designed for research purposes and is not intended to be of direct benefit to you. However, at the end of the study upon your request, you will be provided with feedback on your body fat percent taken during the lab visit.

VI. PAYMENT:

You will be paid $60 for the completed lab visit. During the first hour of your lab visit, we will determine your fasting blood glucose level. If your glucose is >125 mg/dl, then you will be excluded from the study because it is one of our exclusion criteria. However, you will be compensated for your trip to the lab ($20). If you withdraw anytime after this initial glucose check and before completion of the lab visit, you will be compensated with $40 for incomplete blood draws. Payments will be mailed to you after your laboratory visit.

Military: If you are active duty military and wish to be compensated for your participation, you must complete the form "Statement of Approval for Participation in Research" given to you by the study staff. You must inform and seek approval from your Commanders.

Federal Civilian: If you are a federal employee and wish to be compensated for your participation, you must complete the form "Statement of Approval for Participation in Research" given to you by the study staff. If you do not wish to be compensated this form does not apply, but you are strongly encouraged to inform your supervisor of your participation.

VII. RIGHT TO WITHDRAW:

You may decide to stop taking part in the study at any time. Your relations with the faculty, staff, and administration at USUHS will not change in any way if you decide to end your participation. You should let the study leader know if you decide to stop taking part. We also reserve the right to remove you and your sample from the study at our discretion if we determine that circumstances (such as failure to follow instructions, reaction to saline flush, etc) require such actions.

VIII. RECOURSE IN THE EVENT OF INJURY:

This study should not entail any physical or mental risk beyond those described above. We do not expect complications to occur, but if, for any reason, you feel that continuing this study would constitute a hardship for you, we will end your participation in the study.

In the event of a medical emergency while participating in this study or medical treatment is required as a result of your participation in this study, you may receive emergency treatment in the facility you are in or a nearby Department of Defense (military) medical facility (hospital or clinic). Treatment/care will be provided

even if you are not eligible to receive such care. Care will be continued until the medical doctor treating you decides that you are out of immediate danger. If you are not entitled to care in a military facility, you may be transferred to a private civilian hospital. The attending doctor or member of the hospital staff will go over the transfer decision with you before it happens. The military will bill your health insurance for health care you receive which is not part of the study. You will not be personally billed and you WILL NOT be expected to pay for medical care at our hospitals. If you are required to pay a deductible you may make a claim for reimbursement through the Uniformed Services University Office of General Counsel.

In case you need additional care following discharge from the military hospital or clinic, a military health care professional will decide whether your need for care is directly related to being in the study. If your need for care is related to the study, the military may offer you limited health care at its medical facilities. This additional care is not automatic.

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Office of Research at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-3303. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

IX. PRIVACY AND CONFIDENTIALITY:

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Information that you provide and other records related to this study will be accessible to those persons directly involved in conducting this study and members of the Uniformed Services University of the Health Sciences Institutional Review Board (IRB), who provide oversight for protection of human research volunteers. All questionnaires, forms, and charts will be kept in a restricted access, locked cabinet while not in use. Your blood samples, stripped off of any personal information, will be stored in a restricted access freezer over the course of the study (2 years). After verification of the database information, paper copies of all materials containing identifiers will be shredded at the end of the study. Furthermore, published data will contain no references to an identifiable individual. If you are a military member, please be advised that under Federal Law, a military member's confidentiality cannot be strictly guaranteed.

****IF YOU HAVE ANY QUESTIONS PLEASE FEEL FREE TO ASK****

By signing below, you indicate that you have read the explanation of this study on this form. The testing procedures have been reviewed and all your

questions have been answered. You understand the nature of the study and volunteer to participate in it. You attest that you meet the requirements for participation in this study. You understand that the study is designed for research purposes and not to be of direct benefit to you.

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YOU AGREE TO PARTICIPATE IN THE FOLLOWING PROCEDURES:

SCREENING EXAM

BLOOD DRAWING

INGESTION OF A LIQUID MEAL

BODY COMPOSITION EVALUATION

QUESTIONNAIRES

SIGNATURES:

______________________	______________________	__________
Signature of Volunteer	Volunteer Name (Print)	Date

______________________________ ______________________________
Volunteer Address

______________________	______________________	__________
Signature of Witness	Witness Name (Print)	Date

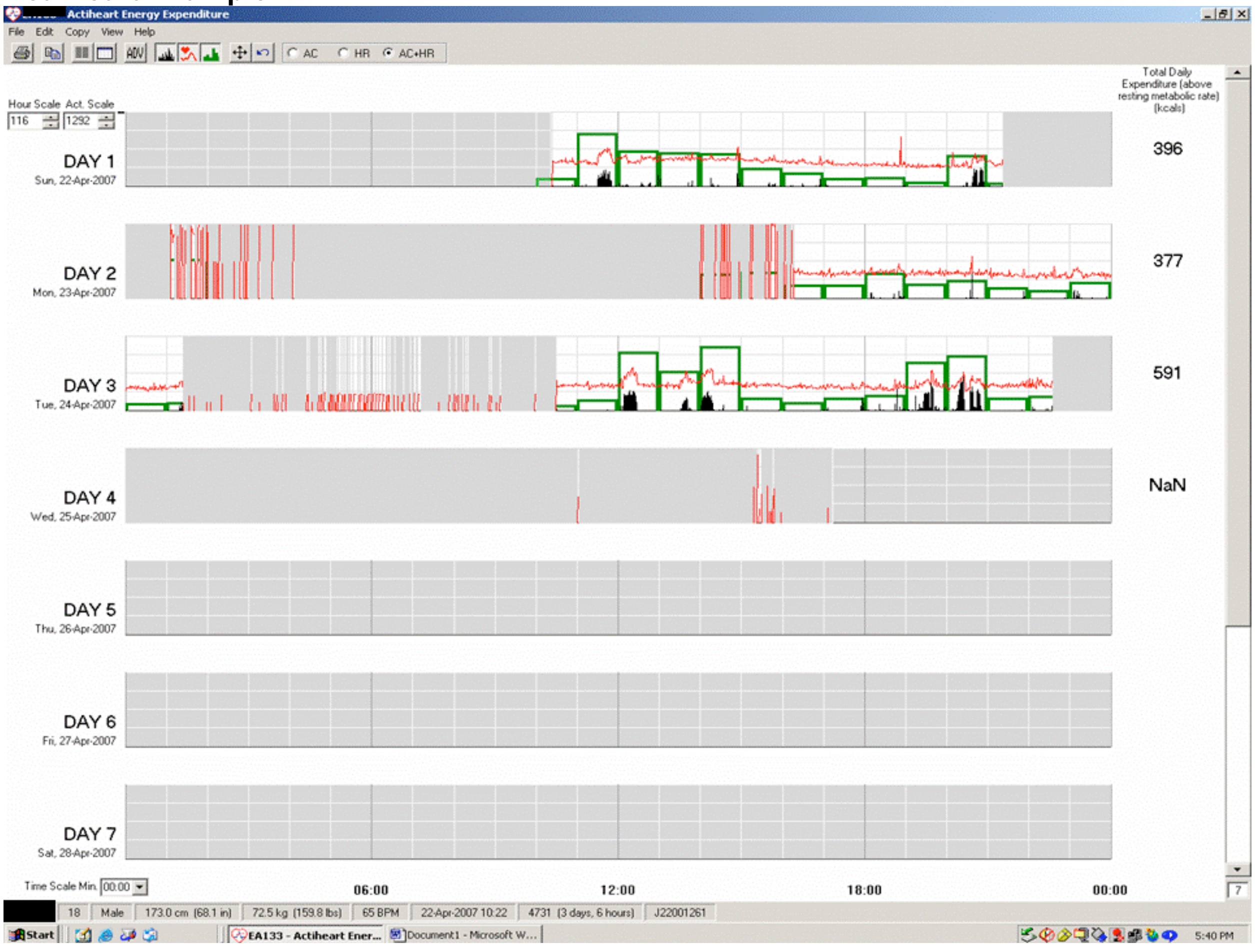
The Principal Investigator certifies that the research study has been explained to the above individual, by the Principal Investigator or a member of the research staff, and that the individual understands the nature and purpose, the possible risks and benefits associated with taking part in this research study. Any questions that have been raised have been answered.

______________________	______________________	__________
Investigator's Signature	Printed Name	Date

Appendix 5

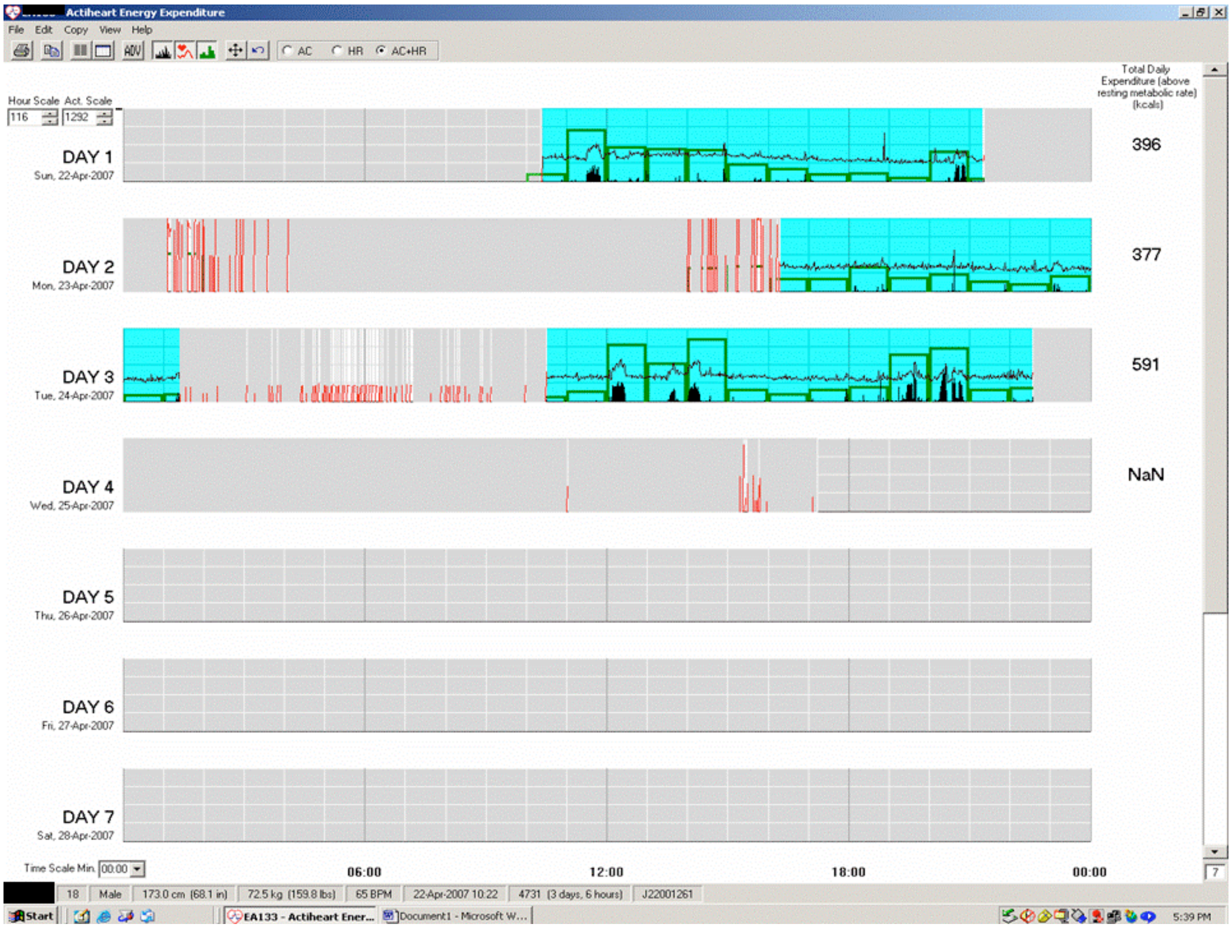
Example of Acti-heart Output and Data Cleaning Process

Acti-heart Example 1



Acti-heart Example 1 is a typical output for heart rate and physical movements. Total energy expenditure and the percent time spent engaged in varying levels of physical activity were calculated from physical activity (black bars) and heart rate (red lines). Participants were instructed to wear the monitoring device for three days, except for during showers/baths, water activities, and sleep. However, as expected, participants wore the Acti-heart for varying time periods each day across the monitoring period. Thus, the segments corresponding to the active intervals of the waking hours were highlighted and total energy expenditure was recalculated; an example is shown in Example 2.

Acti-heart Example 2



In addition, Acti-heart outputs rely on the accuracy of the resting heart rate as measured by the device. The device generates an overall resting heart rate over the monitoring period by averaging the 5-minute interval with the lowest measured heart rate. This overall resting heart rate is then the set point for calculating any and all activity above the resting point (set for 0). However, for a few participants, Acti-heart generated resting heart rates were higher than the laboratory measured resting heart rates. Thus, the output for each participant was examined by comparing the overall resting heart rate to the recorded minimum and the heart rate measured in the laboratory. Resting heart rate values for several individuals were manually

entered so that the laboratory-measured resting heart rate replaced the computer-generated resting heart rate. It is believed that this approach yields more accurate estimate of energy expenditure and percent spent engaged in varying activities.